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THE TREATMENT OF SOME COMMON DERMATOSES OF INFANCY AND CHILDHOOD*

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The treatment of dermatologic diseases in young patients is not difficult if certain fundamental differences in the skin of the child and the adult are kept in mind. These exist especially in the metabolism of proteins, fats, and minerals, and in certain endocrine relations. The chemical composition differs particularly in sodium and potassium ratio and in water content. Nervous and physical reactions are dissimilar. The skin of the child is less oily, possesses less developed hair, less pigment, different secretions, and a more extensive and superficial lymphatic system. Cutaneous reactions during childhood tend to be vesicular, whereas in adults they are more apt to be papular, lichenified, and drier. Immunologic responses also differ.

The delicate, tender skin of the child is more adversely influenced by external factors. Uncleanliness leads to infection; contact with soiled diapers induces irritation. Maternal over-enthusiasm for cleanliness may also produce irritation and excess dryness through frequent bathing, use of strong soaps, medicated oils, and powders. Many mild cutaneous reactions will subside spontaneously if mothers can only be made to realize that every single minor skin abnormality does not require active treatment.

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As in all medical practice, effective therapeutics in pediatric dermatology depends upon correct diagnosis. Prophylaxis is a prime consideration. Care of the skin should not be delegated to the whims of parents or to neighborly advice but should be based on sound medical knowledge. The first essential is cleanliness, attained without disturbing the physiologic and chemical condition of the skin. Oily skin can withstand more frequent washings and stronger (alkaline) soaps than dry skin. Ichthyotic skin requires bathing with oil; seborrheic skin tolerates frequent bathing. Scented oils and soaps are apt to please the mother but will displease the dermatologist, who often is faced with treating resulting sensitizations. Some skins are so delicate that they are irritated by plain water; these may be bathed with isotonic saline solution, nonmedicated (oily) preparations, such as equal parts of olive oil and lime water, or colloidal baths. The latter may be prepared with cornstarch and soda.

Colloidal baths

1. Make a cold water paste of:
   1 cup cornstarch
   ¼ cup baking soda
   and put into about
   ½ tub warm water
   Bathe twenty to thirty minutes, daily, or less often if the skin continues to be dry.
2. Boil 2 cups bulk oatmeal in 1 quart water for 30-45 minutes in a double boiler. Allow to cool for 15 minutes, then add ½ cup baking soda. Pour the

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mixture into gauze bag and tie shut.
Place in a bathtub one-half to three-fourths full of water at about 90-96 F. Patient may remain in tub one-half to two hours, expressing the oatmeal mash through the gauze and applying it to the body. Wash off the mash thoroughly before leaving the tub. Dry by gentle patting, *not* rubbing.

These colloidal baths are excellent in cases of generalized iritations, where soothing measures are indicated. Prolonged use may cause excessive dryness of the skin, which can be corrected by application of olive oil and lime water in equal parts, after bathing. Any attempt to replace natural body oils will be only partially successful at best. Lanolin and aquaphor in various proportions are widely used for lubrication. Too frequent application of oils and ointments to the hairy parts, especially if combined with rubbing, may result in folliculitis.

In general, edematous, erythematous, and exudative eruptions respond to moisture, attained either by wet dressings or baths. After subsidence of the acute process, various powders or lotions may be used. Plain calamine lotion is a convenient way to apply powder to the skin. If this is too drying, a thin coat of a mildly soothing ointment may be applied over the lotion.

An acceptable ointment is:
Boric acid 1.5 (gr. xxii)
Ung. Aq. Rosae q.s. 60.0 (oz. ii)

If the dermatitis has progressed beyond the subacute stage and the skin has become drier, a mildly stimulating mixture may be tried, such as ichthyol, 1 to 3 per cent, in zinc oxide ointment. More stimulating measures should follow, as treatment is tolerated, until complete involution. An excellent keratoplastic is crude coal tar ointment in strength varying from 0.5 to 2 per cent. Exposure to ultra-violet light, carefully increased as tolerated, is highly recommended for more chronic stages.

Treatment must be altered not only for the individual patient but also for different anatomic sites. Ointments should not be employed in intertriginous dermatitis venenata if used in the natural body folds. Ointment applied during the heat of the day rapidly melts, becomes messy, and fast loses therapeutic efficiency. Therefore, the general rule should be to avoid ointments in intertriginous areas and on most cutaneous surfaces during hot weather; lotions, such as calamine lotion, may be substituted. If further antipruritic effect other than drying is desired, 0.5 per cent phenol or 0.25 per cent menthol may be added. Addition of 0.5 to 1.0 per cent ichthyol will produce a mild keratoplastic and some parasiticidal effect.

Treatment of pruritus is necessary not only for relief to the child (and mother) but also for prophylactic reasons. Scratching leads all too frequently to pyoderma. Excoriations are tell-tale signs of pruritus in an uncommunicative patient. Dryness of the skin (asteatosis, xerosis) is probably the most common cause of pruritus. If drying lotions are employed, aggravation will of course ensue. Equal parts of olive oil added to the lotion enhances the soothing effect.

Another useful prescription is:

Menthol	0.3	(gr. v)
Phenol	2.0	(m. xxx)
Olive oil	120.0	(oz. iv)
Lime water	120.0	(oz. iv)
Pulverized zinc oxide	20.0	(dr. v)

SCABIES

Scabies is not diagnosed often in private practice, but many cases go unrecognized. This in part is due to the fact that the disease is ordinarily associated with poor hygiene among underprivileged classes; scabies, like syphilis, however, has no respect for economic or social status. Secondary impetiginous infections increase the importance of this disease in pediatric dermatology. The predominating pyogenic aspects of secondarily infected scabies often obscure the disease. Treatment of scabies itself must often be delayed until secondary infection has subsided. Inef-

ficacy of treatment is usually caused by one of three factors: lack of consideration of reinfection, failure to follow in detail the recommended treatment of the entire skin, or improper disinfestation of clothes and bedding. Parents and siblings should be examined for signs of the disease; if free, they should be isolated and examined periodically until the entire household has been cured. If such examinations are impractical, it is best to treat the entire family.

Although the medical profession is constantly besieged with new, highly publicized scabeticides, the old stand-by, sulphur ointment, still seems to be the most useful and dependable remedy. Variations of the following prescription may be used:

Sulphur precipitate	6.0	(gr. xc)
Balsam Peru	6.0	(gr. xc)
Petrolatum		
Lanolin aa q.s. ad	120.0	(oz. iv.)

Efficacy of treatment depends on detailed attention in its application. Printed forms like the following may be useful:

Observe these rules carefully, and do not repeat the course without your physician's permission, or you may irritate the skin.

First night: A cleansing bath with soap and water to all parts of the body. Follow this with liberal application of the ointment to the skin from the neck downward, including the folds of the body and the regions between the fingers and toes.

Second day: Apply ointment again morning and night under the same clothing. No bath is given.

Third morning: On the following day, or about twelve hours after the third application of ointment, cleanse the skin thoroughly again with a warm soap and water bath. This completes the course.

Clean underwear and bed linen must be used from this point on. It is not necessary to destroy the old clothing; thorough laundering or dry cleaning will do the work. The mite lives not in the clothing but in the skin and is transmitted from one individual to another by close personal contact.

After such a course of treatment, if itching persists, some soothing lotion (such as equal parts of olive oil and lime water) should be applied to the skin. If another course of treatment seems indicated, your doctor should be consulted.

For very delicate, tender skin, a lower concentration of sulphur should be used. Balsam of Peru alone in a petrolatum base may suffice if applied after thorough bathing with soap and water. For infants, a useful prescriptions is:

Storax (USP)	6.0	(gr. xc)
Balsam Peru	6.0	(gr. xc)
Soft white paraffin q.s.	30.0	(oz. i)

Benzyl benzoate is favored by some practitioners. Its use on excoriated scabetic skins often produces undesirable irritation. If it must be employed, treat the inflammatory complicating condition first. In general, this scabeticide is more valuable in treatment of adults. Wash cloths impregnated with sulphur have been used advantageously.

It must be remembered that sulphur is capable of producing a serious dermatitis which may obscure the progress of the disease and produce a condition very resistant to treatment. In such cases of sensitization, after subsidence of the complicating dermatitis, ichthyol in 1 or 2 per cent strength may usually be substituted safely. Pyrethrum also may be used, but it is not an uncommon sensitizer. If sensitization or irritation develops, any energetic scabetic regimen should be abandoned and soothing measures instituted, in the form of daily colloidal baths, followed by application of lotions containing phenol or menthol in an oily vehicle. With subsidence of the complicating irritation, one of the above mentioned alternative measures may be employed. The application of sulphur to the face may irritate the eyes; the very young patient may inadvertently carry sulphur to the eyes by rubbing. If extensive application of the ointment to the hands is necessary, a splint restraint for the arms should be used.

PYODERMAS

Immunity to a number of diseases is transmitted from the mother, but immunity to pyogenic cutaneous disease is a notable exception. For this reason, pyodermas in

infants and young children are often serious and difficult to control. Contact with excreta, exposure to insects, excoriations from scratching or chapping of the skin through improper cleansing, all provide portals of entry for bacteria. The extensive and superficial lymphatics sometimes fail to cope with infection of the skin. Periumbilical infections in infants may have disastrous results.

Impetigo in infancy is a serious disease which may even be fatal. It is highly contagious and spreads rapidly in institutions. Its chronicity, recurrence, and refractiveness to treatment are often embarrassing to the practitioner. Measures that cure impetigo in one patient may fail miserably in another. Ammoniated mercury seems to be more helpful in staphylococcal types, gentian violet in streptococcal. Clinical differentiation may be summarized as follows: The staphylococcal type occurs most frequently in July. The primary lesion is a large vesicle without erythema, which may attain a diameter of 5 cm. It tends to be circinate and to form crusts, is usually of a longer duration and less contagious than the streptococcal type. The latter has a higher incidence in the fall; its primary lesion is of pinhead size and ruptures early. There is a broad erythematous areola, which forms thick yellow crusts; it is extremely contagious but of a shorter duration than that due to staphylococcus.

Ammoniated mercury ointment has withstood the test of time so well that it should be tried first in the treatment of impetigo. A 5 per cent strength is adequate if the drug is going to benefit at all; a stronger percentage will only be irritating. After removal of the non-penetrable crusts, the ointment should be rubbed into the lesions with special attention to the active border. Bandaging with loose mesh gauze but avoiding too much occlusion is advisable. Adhesive tape should not be applied directly to the skin of a patient with impetigo because trauma from removal of the tape spreads the disease. The routine is to apply the ointment at night, remove the crusts in the morning by soaking with soapy water or using wet dressing of mercury bichloride (1:4000). The crusts should be removed as gently as possible: impetigo rarely produces scarring except by excoriations or injudicious treatment. During the day it is customary to use a drying antiseptic preparation. A 1 to 2 per cent aqueous solution of gentian violet is advocated by some, but others object to its staining properties. A currently popular and efficacious product is the alulotion of ammoniated mercury. For infants, this may be diluted with equal parts of Kaomagma and painted on the skin twice a day. If impetigo complicates scabies, prescriptions containing sulphur are desirable. Very extensive and exudative impetiginous patches frequently respond to wet dressings of bichloride of mercury in dilution of 1:4000, applied either continuously or for an hour or more several times daily.

The sulfonamides have been used indiscriminately in treatment of the pyodermas. In view of the serious nature of impetigo in the infant, there is some justification for its use in cases of rapid, extensive involvement. For the few lesions of early impetigo, the previously mentioned measures should suffice; sulfonamides should be reserved for resistant or fulminating cases. It is hardly justifiable to chance sensitization of a very young patient to a valuable lifesaving drug through treatment of a minor skin condition which ordinarily responds to less innocuous measures. Generalized systemic or local sensitization may occur from topical use of these drugs. Sulfonamide rashes may persist for months, preventing valuable exposure to ultraviolet light because of danger of photosensitization. If effective at all, local administration of sulfonamides will produce results in three to ten days. A strength of 5 to 10 per cent may be used in a vanishing cream base or surgical lubricating jelly. Recently, some authors have reported better results with higher concentrations.

The exact effectiveness of penicillin in pyodermas is not known, but many favorable results have been reported. Less dangerous than the sulfonamides, it is the drug

of choice when more than local treatment is indicated. Early administration of 5000 to 10,000 units intramuscularly every two to three hours for as many days should be tried in resistant cases. Fulminating conditions require greater amounts over longer periods. Oral administration of penicillin may be tried for the ambulatory patient. The initial dose is often given intramuscularly in order to raise the blood level rapidly. Maintenance of this level may be attempted orally with two to three times the parenteral dosage. Another plan consists in giving the drug intramuscularly during the day and orally at night. In some clinics penicillin has almost completely replaced former therapeutic measures for impetigo. Locally, the drug may be prescribed in a water soluble base containing 400 to 1000 Oxford units per gram. Deterioration can be reduced by dispensing small amounts and storing at low temperatures. Wet dressings of saline solution in similar concentrations are useful. Economy may be secured through use of washings recovered from discarded ampules. A few reactions to penicillin are known to occur (toxic erythemas, vesiculation, and urticaria), most of which are so mild that treatment need not be interrupted.

MILIARIA
"HEAT RASH"

The nuisance value of miliaria is great; frequently it leads to more serious diseases, such as impetigo and furunculosis, especially in infancy. Little is known about its cause, but it is obviously associated with excessive sweating. Only recently has the physiology of sweating been investigated. Limited pathologic studies have contributed little. Some blame yeast or fungi; others attribute irritation to the perspiration itself. The disease does not seem to be associated with filth *per se*. Unfortunately, the laity ascribes it to infrequent bathing and bathe even more often and more energetically, thereby aggravating the basic condition.

The following concept of the disorder is an interesting one: A fundamental function of the oil of the skin is to protect it from sweat. In hot climates the sebaceous glands are stimulated to protect the skin from sweat. Physiologic imbalance of oil and sweat production in certain individuals may then be responsible for the eruption. Natives of the tropics seem to have a perfect balance of these mechanisms.

Sudamina, a non-inflammatory engorgement of the coil glands, is apparently due entirely to excessive sweating, is more physiologic than pathologic, and requires no treatment. Since the minute vesicles of the disease are superficial, secondary infection need not be feared.

For miliaria, tanning of the skin is often a beneficial prophylactic and even remedial measure. Physical exertion during exposure to the rays of the sun seems detrimental, whereas deliberate gradual exposure for short periods of time may help. In other words, if exposure to sun results in excessive production of sweat, no benefit will be obtained. Bathing should be curtailed, if not completely abolished; certainly long baths, use of hot water and strong soaps should be discouraged. Colloidal baths can easily be substituted. Liberal amounts of cooling fluids should be taken and extra salt added to the diet. Hot fliuds and foods, as well as highly seasoned ones, should be avoided. Sweating and irritation should be minimized by all possible means. In unclothed infants sweat should be removed by blotting the skin with soft absorbent cloths, followed by the application of oil. Obesity should be corrected. Removal of sweat may be secured through powders which induce evaporation by increasing surface area. This is a more desirable method, since exposure to draughts with resultant drying leaves irritating chemical and cellular debris behind. A suitable powder is:

Zinc oxide
Zinc stearate
Talcum aa

This may be used with or without the addition of 4 to 6 per cent camphor. Calamine lotion is convenient. Another less desirable formula is:

Witch hazel

Saturated solution boric acid aa

The use of highly medicated proprietary preparations in the treatment of heat rash is not advisable. The average mother is reticent about consulting her physician for treatment of a simple heat rash; consequently, it is only after a complicating dermatitis venenata or pyoderma develops that she usually seeks aid. Alcohol, through local anesthestic properties, gives temporary relief, but ultimately its drying effect may aggravate the basic condition.

DERMATITIS VENENATA

Treatment of dermatitis venenata is more successful than that of any other group of skin diseases. Success depends largely on early diagnosis, removal of cause, and simple soothing measures.

When an infant starts moving about, the number of possible irritants he may contact increases sharply. A classical example of disease due to external causes is Rhus dermatitis or poison ivy. Dermatitis venenata deserves proper care if for no other reason than avoidance of secondary infection.

Scrubbing with soap and water immediately after contact will remove much of the irritant and thus partially reduce severity of symptoms. Following this, a soothing wet dressing should be applied. Liquor aluminum subacetate (Burrow's solution), in a 0.5 per cent solution, or saturate solution of boric acid may be used. Coop preparations seem most comforting. A roller type dressing of eight to ten thicknesses of wide mesh gauze should be permitted to remain in contact with the skin as long as it is wet. Before completely drying, it should be removed from the affected part, dipped in solution, and reapplied. Pouring the solution over the compresses results in concentration and further irritation. By removing, rinsing, and changing gauze, excreta and debris from the area will be carried away. Undue maceration may be prevented by allowing the skin to dry for about fifteen minutes every two to three hours. Frequent or continuous collodial baths are also indicated.

There is some controversy as to whether or not vesicles and bullae should be opened. In climates where pyodermas are prevalent, the vesicles should be opened in an attempt to prevent secondary infection; otherwise bacteria in the superficial layers of the skin find an excellent culture media in the contained serum. If infection should develop, debridement is essential. For complicating infections a good wet dressing consists of 1:12,000 potassium permanganate; this is soothing, drying, and antiseptic. When involvement is extensive, baths with this solution in a dilution of 1:20,000 are helpful. Weak solutions of bichloride of mercury or silver nitrate may also be used.

Desensitization either with elixir of the Rhus product or by parenteral administration of the oily substance of the plant should be avoided during the acute stage. Favorable results doubtless occur, but the probability of dissemination makes this practice hazardous at this stage. It should be reserved for prophylaxis prior to anticipated contact, and even here its value is questionable. The favorite home remedy of chewing the leaves may have obvious disastrous results! Recent attempts at oral desensitization by use of capsules containing the oil have possibly effected some benefit but have also produced a number of instances of perianal dermatitis venenata. A familiar complication of an old, well accepted therapeutic measure is the tattooing ensuing from the use of iron-containing preparations. The best advice a practitioner can conscientiously give a sufferer is: "Leaves three, let it be."

Any discussion of this group of diseases must include a common, readily avoidable and easily treated one, ammoniacal dermatitis. Urea in the urine decomposes into ammonia by action of saprophytic bacilli from the stool, giving rise to a characteristic smell and irritative dermatitis. Use of coarse, rough, improperly laundered diapers sets the stage. Consequences may be so severe as to cause retention of urine either by occlusion of the urethral meatus or voluntary withholding of urine because of pain. Prophylaxis consists of avoidance of overfeeding and resultant diarrheas,

frequent diapering with soft clean material, and proper laundering. The diapers should be finally rinsed in a saturated solution of boric acid. Drying lotions, dusting powders, and oil inunctions are also beneficial.

LANATOSIDE C (CEDILANID)

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As William Withering, the father of digitalis therapy, said many years ago, "It is much easier to write upon a disease than upon a remedy. The former is in the hands of nature, and a faithful observer, with an eye of tolerable judgment cannot fail to delineate a likeness. The latter will ever be subject to the whims, the inaccuracies and the blunders of mankind." By way of definition, however, it may be stated that cedilanid is a pure, stable, crystalline, adequately soluble, constant in action, lanatoside C, one of the principal clycosides of Digitalis lanata. Cedilanid is the trade name for this preparation. It must be added that this glycoside is not present in Digitalis purpurea.

The purpose of this paper is to discuss briefly the following points: (1) The chemistry of the cardiac glycosides, with special reference to cedilanid; (2) the cardiovascular actions of cedilanid and comparison with some of the other glycosides; (3) the routes of administration, their indications and dosage; (4) some aspects of toxicity.

CHEMISTRY

Medicine is deeply indebted to Stoll[1] and his co-workers for the brilliant work regarding the chemistry of the cardiac glycosides. Previous to the work of this author, much confusion was present regarding the true chemical nature of these substances. Stoll defines the "genuine glycosides" as "the unchanged initial cardiac glycosides as they pre-exist in the fresh plant, carefully dried," and consist of an aglucone nucleus linked by a side chain to a various number of sugars. The glycosides as previously known were shown to be degeneration products of the genuine glycosides, some of the sugar molecules having been lost. This author, using a special process, was able to extract the genuine glycoside complex, Digilanid, from which the pure crystalline genuine glycosides, the lanatosides A, B, and C were subsequently extracted. These glycosides can be determined gravimetrically, thus obviating the necessity for bio-assay, as well as containing no enzymes so that no change in potency results from storage.

Further, Stoll[1] found in studies on Digitalis purpurea two amorphous initial glycosides chemically related to lanatosides A and B, corresponding to the previously known digitoxin and gitoxin respectively, the latter being deficient in a glucose molecule. On the other hand, lanatoside C, corresponding to digoxin in a similar manner has no chemical counterpart in the glycosides of Digitalis purpurea. Thus it is seen that lanatoside C is a genuine glycoside differing chemically from all other known glycosides, and existing in a crystalline state, and hence stable, adequately soluble, and constant in action. (See Fig. I for interrelationships of the glycosides.)

Chen and co-workers[2] state that the removal of a sugar from the glycoside molecule diminishes the persistence of action of the drug. They state further that each aglycone has a less powerful effect on the heart than its parent glycoside. Also it was found that the aglycone had a higher emetic action than the parent glycosides.

Gold[3] disagrees diametrically with Chen and using the human assay method found that:

(1) Digitoxin (Digitaline nativelle) was ten times and gitalin four times more potent than digitalis leaf or cedilanid.

(2) As to absorpition the ratio between the oral and intravenous dose is ten to one for cedilanid, one to one for digitoxin, and five to one for digifoline. It must be remembered, however, that here rate of destruction and elimination is included. Further, Sokolow and Chamberlain[4] on the other hand found this ratio of oral to intravenous dose to be only 1 to 2.8. Dille and Whatmore[5] in a series of experiments in which cats with isolated loops of stomach, intestine (ileum and jejunum) and colon with

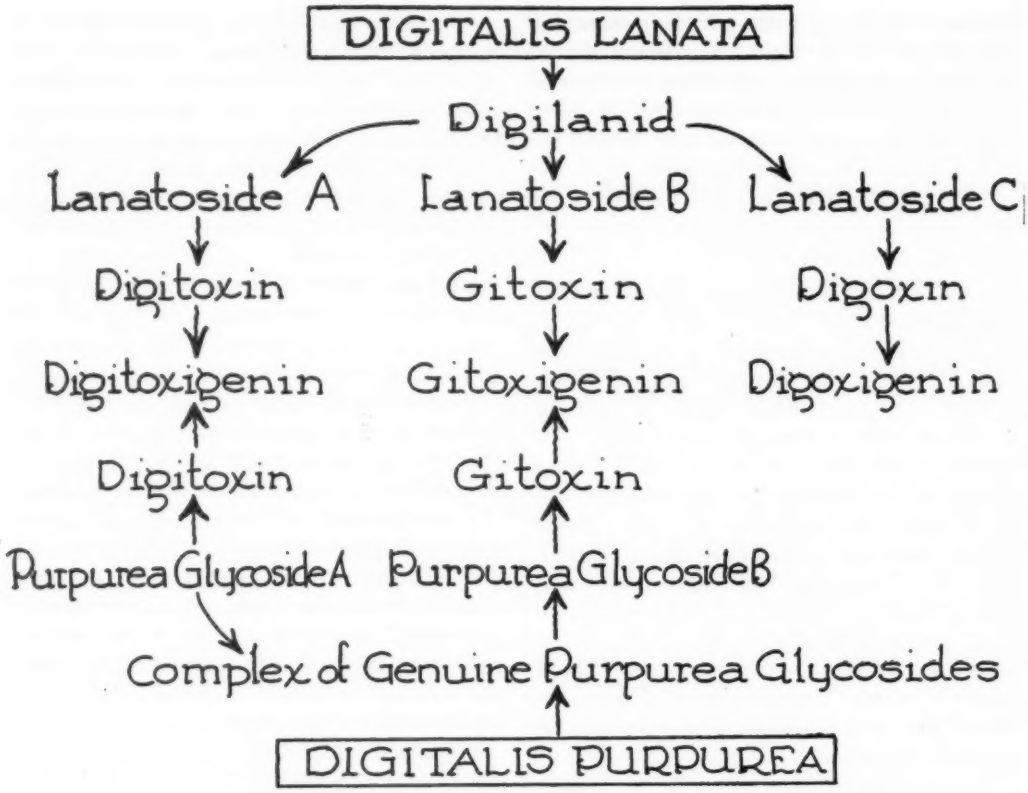

Fig. 1. Chemical relationships between the glycosides of Digitalis lanata and purpurae (modified from Sokolow and Chamberlain[4] after Stoll and Kreis).

their blood supplies intact were used, cedilanid and tincture of Digitalis U.S.P. XI were injected into the lumen; after one hour the loop of gut was removed and bioassayed on frogs while the cats received intravenous infusions containing the same drug to point of death.

By this method they found greatest absorption of both drugs from intestine (about three times as much as from stomach or colon.) Also cedilanid was found to be absorbed about three times as rapidly from the intestine as tincture of digitalis (determined by varying the length of absorption.)

Discrepancies were found between the calculated essential absorption and the apparent absorption which is indicative of partial destruction or inactivation of both drugs in the lumen of the gastrointestinal tract by digestive enzymes.

(3) As to speed of action Gold[3] found that: (a) the oral action varies with speed of absorption and: (b) that by means of intravenous administration ouabain digitalizes the patient within two hours, digitoxin in six hours, with cedilanid falling somewhere between the two. Fahr and LaDue[6] found that cedilanid administered intravenously to patients with auricular fibrillation reduced the heart rate to normal within a period of from two minutes to two hours, and when administered orally within 24 to 48 hours.

(4) Concerning speed of elimination, Gold[3] states that ouabin and cedilanid have about the same rate, that is, less than two-thirds of the effect being lost in four days, whereas with digitoxin less than one-third of the effect is lost in four days.

DeGraff and Lehman[7] have pointed out

that there may be some qualitative difference between various cardiac glycosides. They state, "The lethal effect of lanatoside C dissipates rapidly during the first 24 hours after intravenous injection in the cat. The lethality of digitoxin, however, actually increases during the first three hours and is still quite strong after 24 hours. This very considerable qualitative difference between the action of the genuine glycoside and the product of its partial hydrolytic degradation appears not to have been emphasized before. As would be expected, the effect of digoxigenin completely disappears in 24 hours. At three hours, however, digoxigenin causes an increased tolerance for ouabin. Further investigation is needed to determine the significance of this finding." The interesting, if somewhat confusing, conclusions of these authors may, however, point the way for future investigation along this line.

CARDIOVASCULAR ACTIONS

It has long been recognized that the primary and most important action of the cardiac glycoside is that of increasing the force of the systolic contractions of the heart. Gold[8] using the papillary muscle of the cat performed a series of experiments in which all the secondary factors which may affect the diastolic heart size were removed. It was found that digitalis does not influence the length of the resting fiber, but merely causes increased force of contractions. Investigating the theory that Starling's law was effective up to a certain point above which over-distention occurs, the author, using cats, occluded the aorta and caused intra-auricular pressure to rise to 100 cm. of water. However, this failing and distended heart thus produced still obeyed the normal law, that is, with a lowering of venous pressure, the force of contraction declined and with a raising of the venous pressure, the force increased. Studies by others in man exhibit the same so that there is no reason for assuming that in clinical heart failure the muscle is overstretched or that making the muscle smaller with digitalis will improve its function. Thus it is seen that the decrease in heart size is entirely secondary to improved systolic force rather than being its cause. These experiments may be criticized because of the absence of physiologic conditions, as well as the fact that myocardium from experimental animals rather than humans was studied. LaDue and Fahr[9], believing with Cohn and Stewart that the decrease in diastolic heart size was important, studied this action in a group of patients and reached the following conclusions which are quoted directly because of their importance and clarity of meaning.

"1. The intravenous administration of lanatoside C. to patients with heart failure and normal sinus rhythm usually increases the pulse pressure and reduces the circulation time and venous pressure within two hours. Roentgenkymographic studies of the hearts of ten such patients showed that the drug produced a significant reduction of diastolic heart volume in five patients and an increase of stroke output in eight patients. In two patients, the minute volume of the heart was so large before the administration of the drug that no great increase could be expected.

"2. In the eight patients who responded with increased cardiac output the product of the stroke output and the mean blood pressure was definitely increased, whereas the diastolic heart volume decreased or was unchanged. Since the diastolic heart volume is an index of oxygen consumption, these increases in work which resulted from the administration of lanatoside C. must have represented proportional improvement in the mechanical efficiency of the hearts of eight of the ten patients studied.

"3. In seven patients who were restudied after the establishment of compensation, there was a decrease of 200 c.c. or more in the diastolic heart volume. In four patients, the minute volume was greater than at the start of the experiment, and in three patients it was less.

"4. The most consistent and lasting change in the failing heart that is produced by the administration of lanatoside C. seems to be a decrease in its diastolic volume, or oxygen consumption."

Perhaps a fair evaluation of the work done to date would be that all other important effects of the cardiac glycosides are probably secondary to an increase in the force of systolic contraction and its accompanying improved ventricular emptying.

The mechanism by which digitalis causes a slowing of heart rate has long been a subject of debate. Gold and coworkers, [8, 10] in reviewing the literature on this subject, found that whereas Cushney believed that in auricular fibrillation digitalis slowed the heart by its action directly upon A-V conduction and Lewis thought the action was largely through the vagus, Elsie Porter thought the action was entirely through the vagus. Gold found that in the human both factors are active, with passage from the vagal to the extravagal form of slowing as the drug is increased and in the reverse direction as the drug is eliminated. The vagus is found to be stimulated reflexly as a result of improved myocardial function. Quoting Gold[8], "The problem of control of heart rate in patients with auricular fibrillation, which rises during free physical exercise even though satisfactory 'rest digitalization' is present, has a direct bearing on the vagal-extravagal question. It was found that in patients receiving (1) no digitalis, (2) moderate doses of digitalis, and (3) large doses of digitalis, atropine intravenously in doses sufficient to block the vagus has the same effect in increasing the rate in all three groups as did climbing stairs to the limit of endurance. Digitalization to the extravagal extent prevented this increase in rate, although in some cases the dosage required was quite close to that which causes impaired appetite and nausea."

Gold[10] further found that which of the two factors, that is, vagal or extravagal, predominates is entirely a function of the degree of digitalization and not a matter of individual peculiarity, degree of heart failure, or the length of time the heart has been under digitalis. The maximum effective dose of atropine for determining which factor predominates was found to be gr. 1/30 given intravenously every five to six hours. It is readily seen that the use of atropine to determine the degree to which a patient is digitalized may be of great value, specially when one is using potent intravenous glycosides.

Further discussion as to the effect of digitalis on diastolic heart size, cardiac output, venous pressure, blood pressure and diuresis, in humans, is beyond the scope of this paper. However, the effect of the glycosides upon coronary circulation is of considerable importance. LaDue[11] found that whereas Essex and Visscher had shown that lanatoside C in therapeutic doses does not restrict coronary flow as measured by the thermostromuhr, myocardial damage may be produced in the hearts of dogs by the daily intravenous injections of doses of cedilanid greater than 0.20 cat units per kilogram of body weight. The fact that no gross or microscopic abnormalities were found in the coronary vessels even in the presence of subendocardial hemorrhages in animals who died after these injections points to the probability that cedilanid must exert a powerful vasoconstrictor action on the vessels in large doses. This point will be dealt with further under toxicity.

As to the electrocardiographic changes produced by the various digitalis preparations, it is common knowledge that T wave changes as well as shifts in the S-T segment are always present. An interesting study by Tandowsky[12] revealed that the average time required for the production of maximal RS-T segment changes after the administration of 1.6 mg. of cedilanid intravenously (this being the usual digitalizing dose recommended) was 27.5 minutes in persons with normal hearts as compared with six hours and fifteen minutes, after a single oral dose of 16 grains of Digitalis purpurea. In patients with congestive failure treated similarly intravenous cedilanid produced maximum changes in the RS-T segment in two to three hours whereas oral Digitalis purpurea did so in thirteen to fifteen hours. In the normal control group RS-T changes returned to normal in about sixteen hours after the single intravenous dose of cedilanid and in 48 hours, after the

single oral dose of Digitalis purpurea. Tandowsky further observed that with intravenous cedilanid the clinical manifestation of congestive failure disappeared more rapidly than with the oral leaf and that the emetic quality of the leaf was almost entirely absent with intravenous cedilanid.

ROUTES OF ADMINISTRATION, THEIR INDICATIONS, AND DOSAGES

The indications for the oral use of cardiac glycosides are so obvious that they will only be listed:

(1) Congestive heart failure, from any cause whatever, is the true primary indication for digitalis.

(2) Arrhythmias: (a) Auricular fibrillation or flutter with or without heart failure; (b) paroxysmal tachycardia with impending failure.

Whenever the subject of dosage arises in regard to the cardiac glycosides, the question of bio-assay immediately presents itself. Suffice it to say that Gold[8], and his coworkers,[13, 14] have led the way in replacing the frog method of U.S.P. XI with the far more accurate (as to potency in man) cat method of Hatcher and Brody which became official in U.S.P. XII. Possibly nowhere in medicine, however, is the value of gravimetric dosage of a drug more important than in the use of cardiac glycosides. Only through the use of human bio-assay as advocated by Gold and Cattell[13] can the potency of the pure glycosides be determined but once these values have been ascertained the clinician will be relieved of the alarming toxicity which has so frequently manifested itself with the use of crude drugs in the past. The human bio-assay has been criticized as employing unphysiologic criteria (that is, ventricular rate changes in patients with auricular fibrillation and T-wave changes in patients with regular sinus rhythm), but these criteria are certainly the most objective and easily measured effects yet found and Gold[15] has applied his findings to over 1000 patients and shown them to be satisfactory, at least in his own estimation.

The remainder of this section will be limited in extent largely to the discussion of four representative digitalis preparations: the whole leaf of Digitalis purpurea, cedilanid, digitoxin, and ouabain. The principles stated here may be applied to various other preparations, but as most cardiologists agree, the clinician should familiarize himself with a few of the available digitalis preparations and learn what can be expected from their use in order that the danger of becoming lost in the maze of high pressure propaganda and grandiose claims made from time to time by the various drug houses may be obviated. All doses will be stated in the metric system since the greatest universality of measuring and understanding is thus attained.

Using cedilanid orally for digitalization, Fahr and LaDue[6] advise giving 3.75 mg. at once, followed by 2.5 mg. in the next 12 to 24 hours in single or divided dosage. Sokolow and Chamberlain[4] recommend 7.5 mg. given in three days and Gold[15] found that 1.5 to 2.5 mg. daily gave good results. It should be stated that cedilanid is marketed in 0.25 mg. and 0.5 mg. tablets so that ease of administration is facilitated.

Using digitoxin (Digitaline nativelle) Gold[15] in 1000 unselected cases found that 1.2 mg. in a single dose served to digitalize the patients in from six to ten hours with almost no toxic effects. This dose is equivalent to 1.2 gm. of the leaf which requires 24 to 48 hours for digitalization since it cannot be given at one time because the local gastrointestinal irritation will cause nausea or vomiting in 10 to 20 per cent of the cases. An alternate regime using digitoxin is 0.2 mg. every four to six hours if slower action is preferred. The fact that digitoxin is completely absorbed from the gastrointestinal tract, thus making the oral and intravenous dose the same, is a strong argument in favor of the use of this drug for routine oral digitalization in preference to cedilanid which is only one-tenth (Gold[15]) or one-third (Sokolow and Chamberlain[4]) absorbed from the gastrointestinal tract.

As to oral maintenance dosages, an average of 1.5 mg. of cedilanid, 0.1 to 0.2 mg. of digitoxin, or 0.3 gm. of the leaf is re-

quired. Ouabain and strophanthin are, of course, given only intravenously.

The indications for intravenous digitalization are as variable as the number of men writing on the subject. LaDue[16] states that in Europe where strophanthin (or ouabain) has been used much more widely than in the United States, the indications are: (1) Acute failure of a high degree, that is, cardiac asthma; (2) slowly progressive failure with acute distress; (3) for patients unable to take digitalis orally. Pick[17] states that intravenous strophanthin is indicated in: (1) Acute cardiac insufficiency due to previously untreated hypertensive disease; (2) mitral stenosis during delivery; (3) coronary diseases developing acute pulmonary edema and nephritis; (4) paroxysmal tachycardia with rapid onset of decompensation.

He states that the only contraindication to intravenous strophanthin therapy is previous digitalization. For the experience of one clinician in the use of ouabain and a comparison of its value with that of digitalis in the treatment of heart failure, the reader is referred to an excellent article by Chavez[30] of Mexico City, in which physicians of the United States are vehemently criticized for having neglected the use of ouabain while it was being used to great advantage in Europe and Latin America. This view is not shared by LaDue[16] who warns that strophanthin is a dangerous drug because of the incidence of toxicity including: (1) uncontrollable nausea and vomiting; (2) heart block; (3) cardiac standstill; (4) ventricular tachycardia, and (5) ventricular standstill. I feel unqualified to evaluate these representative views which are so extremely contradictory.

Pick,[17] however, states that intravenous cedilanid more closely approaches strophanthin as to rapidity of action and weaker cumulation than any of the other available digitalis glycosides and has the added advantages of great therapeutic breadth and a remarkable diuretic action.

Tandowsky[12] writes that intravenous cedilanid is indicated: (1) When the element of time is an important consideration in the treatment of congestive failure, that is, moribund patients; (2) for patients who are suffering from nausea and vomiting when rapid digitalization is indicated; (3) in auricular fibrillation with congestive failure, since he found that three of 11 patients regained a normal rhythm in a group so treated whereas none of the group digitalized with oral leaf regained a normal rhythm.

Investigating the oft-stated contraindication to intravenous digitalization, that is, previous use of oral digitalis within three weeks, Ray and La Due[18] found that the absence of toxic manifestations and the definite improvement evidenced after the intravenous use of cedilanid in patients taking digitalis leaf before and during the onset of failure, suggested several conclusions which are quoted directly. "Since the rate of improvement was more rapid than that to be expected from bed rest alone, it seems obvious that these patients were not receiving adequate therapeutic amounts of digitalis. A combination of factors may explain the tolerance of these patients to the intravenous administration of lanatoside C. The need for more digitalis when heart failure occurs, no matter what the precipitating factor, plus the possibility that the destruction and elimination of the digitalis accumulated during the period of 'digitalization' contributed to the onset of congestive failure.

"From our results, it would seem to be reasonably safe and usually of therapeutic benefit to give 0.4 to 0.8 mg. of lanatoside C intravenously to patients who develop congestive heart failure while taking maintenance doses of from 0.1 to 0.3 gm. of folia digitalis.

"Finally this study indicates that the mere finding of 'digitalis effect' in the electrocardiogram is apparently not proof that the patient is receiving adequate therapeutic doses of the drug.

"1. The intravenous administration of from one-half to the full digitalizing dose of lanatoside C to patients developing congestive heart failure while taking maintenance

doses of Digitalis purpurea was followed by definite improvement in forty-six of the sixty-two patients so treated.

2. Objective evidence of improvement was shown by thirty-six of forty-nine patients with regular sinus rhythm and by ten of sixteen patients with auricular fibrillation.

"3. There was only one toxic reaction among the sixty-two patients.

"4. The presence of electrocardiographic evidence of 'digitalis effect' is not proof that therapeutic amounts of digitalis are present in the body (the authors[10] used the atropine test alluded to above).

"5. The mortality of the patients studied was no greater than that previously observed[6] in a group of patients with heart failure of comparable severity who had not been taking digitalis within three weeks prior to intravenous digitalization.

"6. None of the deaths occurring during this investigation could be attributed to the intravenous administration of lanatoside C."

As an addendum to this paper, Ray and LaDue[18] stated, "Since submission of this manuscript, thirty-five patients with sinus rhythm and fifteen patients with auricular fibrillation have been added to the series. There were no toxic manifestations in the patients with auricular fibrillation; six of the patients with regular sinus rhythm developed transient toxic reactions. Thus of 104 patients with regular sinus rhythm, seven, or 6.7 per cent, developed nausea, emesis, and occasional extrasystoles. None of the patients with auricular fibrillation experienced toxic reactions and no deaths could be attributed to the administration of the drug."

This beautiful piece of clinical investigation may be criticized in that no control group was used, but certainly it indicates that many of the alleged accidents and poor results with intravenous cedilanid are mere heresay and not based on scientific medical facts.

If further clinical testimonials as to the value and safety of intravenous cedilanid are desired, the reader is referred to papers by Chamberlain and Sokolow,[19] Sokolow and Chamberlain,[20] Nicholson,[21] Margolin,[22] and Hrenoff.[23]

The dosage by intravenous injection for cedilanid is 1.6 mg. in a single dose, this being 8 cc. of the solution available in 2 cc. and 4 cc. ampules, or an alternative of 0.8 mg. followed in two hours by 0.8 mg. For ouabain the dosage is 0.25 mg. which may be repeated in two hours if required. For digitoxin the intravenous is the same as the oral dose, 1.2 mg. in a single dose.

Intramusclar injection of cedilanid may be used but is often accompanied by local pain and discomfort so that it is seldom recommended or indicated.

Rectal administrations of tincture of digitalis diluted 1:7 or powdered digitalis as suppositories may be used in the same dosage as the oral; cedilanid is not available in suppositories.

With an eye to the future as to some possible "special indications" for cedilanid in preference to other glycosides, the following statements are presented for the readers' evaluation. Several authors,[4, 12, 24] have suggested a relatively high incidence of return to normal rhythm in patients with auricular flutter of fibrillation or supraventricular tachycardia in patients receiving intravenous cedilanid as compared with Digitalis purpurea although no well-controlled studies along this line have been made.

Fahr and LaDue[6] controlled the heart rate and reduced venous pressure from 22 to 9 cm. of water in 48 hours in one patient with auricular fibrillation from hyperthyroidism who failed to respond to the leaf.

Erickson and Fahr[25] advocate the use of cedilanid orally in organically diseased hearts which appear compensated when the circulation time by the calcium gluconate arm-to-mouth method is greater than 16 seconds. This regimen is reputed to do no harm and is beneficial to many cases with circulation times of less than 16 seconds, and it is felt by these authors that life expectancy may be increased as well as physi-

cal fitness and that congestive failure may be prevented for a period of years.

Tandowsky[26] suggests that paroxysmal auricular arrhythmias may be stopped by intravenous cedilanid and then the drug may be used orally in doses of 0.5 to 1.0 mg. daily (varying with electrocardiographic effects) as a prophylactic against recurrence of the paroxysms.

TOXICITY

Since this subject has been touched upon many times earlier in this presentation, only brief additions will be made. The toxic effects of strophanthin have already been listed and those for the leaf are familiar to all, that is, nausea and vomiting, diarrhea, and almost any known clinical cardiac arrhythmia with "coupling" or bigeminy and extrasystoles seen most frequently.

Cedilanid has been shown to produce most of the toxic manifestations. Whereas Moe and Visscher[27] concluded that lanatoside C had thirty times as great a ratio of the toxic to therapeutic dose as lanatoside B, they were, as was pointed out by Gold and Cattell[13] comparing concentration in heart-lung preparations to the fatal intravenous dose in cats. Comparing ouabain, digitoxin and the three lanatosides (A, B, and C) by the papillary muscle technic, Gold and Cattell[13] found the toxic to therapeutic ratios about the same for all; and using oral administration to man the percentage incidence of toxicity for full therapeutic and double therapeutic doses of leaf, digitoxin and cedilanid were found to be the same for all three.

LaDue's studies[11] on coronary spasm in dogs caused by massive doses of cedilanid intravenously have been described. In a later article LaDue[28] reported that whereas prolonged daily oral administration of leaf or cedilanid in doses one and a half to ten times those given for clinical maintenance produced no morphologic changes in the hearts of dogs; daily intravenous doses of 0.2 mg. or more of cedilanid per kilogram of body weight gave necrosis, fibrosis and atrophy of the myocardium in 44 per cent of the dogs suitable for study but there was no correlation between electrocardiographic changes and the appearance of the myocardium in the fifteen dogs so studied. One important point which may have clinical significance is that a group of dogs receiving 0.5 mg./kg. of cedilanid intravenously daily plus 1.5 mg. of atropine sulfate subcutaneously twice daily lived three times as long as dogs receiving the same doses of cedilanid and no atropine. The fact that in the former group (given atropine), sialorrhea, anorexia, and emesis were inhibited is cited as indicating that vagal inhibition prolonged life in dogs receiving cardiotoxic doses of cedilanid.

Rosenblum et al.[29] in a small group of dogs confirmed the work of LaDue,[11, 28] as to the production of myocardial necrosis from prolonged intravenous cedilanid, six out of eight dogs showing focal necrosis but in addition he found that each of two dogs given digitoxin intravenously had even more necrosis. This series is probably not conclusive because of the small number of animals involved.

SUMMARY

A critcal survey of the literature regarding many phases of experimental study on the cardiac glycosides with special reference to lanatoside C (cedilanid) has been presented, together with an attempt at fitting together the picture of the importance of these experimental findings as regards clinical medicine.

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CONGENITAL CYSTIC DISEASE OF THE LUNG

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SYNONYMS

Because of the variety of terms used in the past in discussions on congenital cystic disease of the lung, it is important to record them in order not to lose contact with the earlier records of this condition. I have found eighteen different terms in the literature that I have read and there are undoubtedly others. They are: (1) congenital cystic disease of the lung, (2) congenital cystic formation of the lung, (3) congenital cystic malformation of the lung, (4) atelectatic bronchiectasis, (5) congenital bronchiectasis, (6) honeycomb lung, (7) pulmonary cysts, (8) emphysematous bullae, (9) vesicular pulmonary emphysema, (10) bullous emphysema, (11) pleural blebs, (12) chronic interstitial pneumonitis with emphysema, (13) pulmonary pneumatoceles, (14) pneumatocele, (15) pneumocele, (16) pneumocyst, (17) air cyst, and (18) balloon cyst of the lung.

DEFINITION AND CLASSIFICATION

Congenital cystic disease of the lung is difficult to define because of its variety of types and manifestations. It might be defined as any congenital cystic condition connected with the respiratory tree. It may or may not be symptomatic, depending on the amount of lung tissue displaced and on the presence or absence of infection. It may be bilateral or unilateral. The cysts may be single or multiple and may or may not contain liquid.

I shall present two classifications; namely those of Koontz and Sellers.

Koontz's Classification

"a. Bronchial dilations, as shown by the concentric muscle fibers in the walls, cartilage at times, and the lining of stratified ciliated columnar epithelium.

"b. Cavities resembling emphysematous blebs lying subpleurally."

Sellers' Classification (modified from Cheney and Garland)

1. Solitary cysts—almost invariably of large size

   a. Huge "balloon" or "distention" cysts in infants causing gross pressure signs and often death.

   b. Smaller cysts about the size of an orange. These are often silent clinically unless they become infected.

2. Multiple cysts of varying size

a. Medium size, in groups of two or three close to the root of the lung. These are cherry to golf ball size, usually not clinically noted.

b. Small cysts, of currant to cherry size.

1. Following a set distribution usually lobar ni character. Conformity in size of cysts (honeycomb lung).

2. Diffuse or scattered lesions with cysts inconstant in size.

Neither of these classifications includes the congenital buds from the primitive foregut which are lined by gastric or intestinal mucosa.

HISTORY

The first mention of this condition was in 1638 in a report from Fontanus to Claudius Plempius. In 1687 Thomas Bartholinus reported three cases of congenital cystic disease of the lung and included this original case in the three. The patient was said to have died because the heart could not be properly cooled by the air from this vesicle.

Until 1925 the condition has been of academic interest only. In this year Koontz reviewed the literature and found 108 cases reported since the seventeenth century. None of these were in the American literature. In 1937 Schenck found 381 cases, an increase of 243 cases in twelve years. The wide use of the x-ray, especially in the Army and Navy and in routine examination for tuberculosis and the rapid advances in thoracic surgery, have caused universal interest in this condition. Reports are not at all uncommon now.

INCIDENCE

Congenital lung cysts are of equal incidence in both sexes. There have been reported cases in ages varying from premature infants to extreme old age. There is a difference of opinion as to the incidence. Pierce says that a true congenital cyst is a "rara avis." Greaves states that the increased incidence is due to the increased search for tuberculosis. No doubt there are numerous cases of cystic disease of the lung that are unrecognized when present in an x-ray. There are also many people whose cysts cause them no symptoms and therefore they are never diagnosed. It would be very difficult to determine the actual incidence. There has been a marked increase in incidence of reported cases since Koontz's paper in 1925. Brown and Brock state that the highest incidence of symptomatic cysts is in infants.

If those cases, wrongly diagnosed as types of bronchiectasis and as other conditions, were included the incidence would be much higher.

ETIOLOGY AND PATHOLOGY

The etiology of congenital cystic disease of the lung is not definitely known. This is shown by the great number of theories as to its cause. It is agreed by most authorities that the condition is congenital. The fact that when the condition is discovered in old age and the lung collapsed by the cyst is examined it does not show any pigmentation which lung tissue that has functioned shows. This proves that the lung was collapsed before birth.

I shall give a short statement as to the various causes as advanced by several different men who have given opinions as to the cause of the disease.

Grawitz believes that the condition is due to "hydroptic cystic malformation" due to faulty anlagen of the lymph system of the involved portions of the lung. The cysts, according to him, are of this origin.

Stoerk states that there are two types of cystic disease of the lung: (a) that due to fetal bronchiectasis secondary to infection with stenosis and closure of the bronchioles of the fetus. The cysts are said to be due to the collection of secretion distal to these obstructions; (b) that due to the excessive growth of the parts surrounding the bronchial tree, especially the connective tissue with retention of the fetal characteristics, that is, blunt, stubby tubes.

Sandoz puts forth the idea that it is due to faulty alveolar development from the small end bulbs of the bronchial tree in the embryo. He attributes this to congenital lues.

Kimla attributes the development of congenital lung cysts to excessive growth of

the mesodermic structures with a parceling out of the glandular structures, which then undergo cystadenomatous change.

Couvelaire's idea is that endoderm is the essential factor necessary and sufficient for cyst formation.

Buchmann stated that the cysts were really tumor changes as shown by the strong development of the smooth muscle and epithelial proliferation.

Humbert, along with Balzer and Grandhomme, thought that syphilis played an important part in the development of lung cysts and that if the condition was not present at birth, it might develop later due to some congenital defect.

According to Heuter, the cysts develop because of a closing off or stenosis of the bronchial branches. He stated that the earlier the process develops, the fewer and larger the cysts. If the process develops late the cysts are more numerous and smaller. This idea is similar to that of Stoerk.

Heller said that it was a result of faulty expansion of lungs which were normal at birth.

Oudendal thought that the regular character of the cyst wall showed that it was not a neoplasm. He thought that fetal adhesions caused the cystic condition.

Box attributed the condition to bronchopneumonia.

Kanthuch and Rolleston described the cyst cavities as being broken down abscess cavities, but at the same time they described the walls as being smooth and glistening.

King and Harris think that the bronchi develop as small ramifications of entodermal tissue which become canalized. According to them this canalization occurs distal to some noncanalized part and the mucosa secretes mucous and causes the development of a cyst.

Most of the theories as to the cause of cystic disease of the lung are included in the above theories. Some are parts of more than one of the above.

As has already been stated in the classification, the cysts may be single or multiple, large or small and fluid containing or air containing.

Koontz found an incidence of 50 per cent in the left lung, 25 per cent in the right lung and 25 per cent in both lungs.

Schenck found 38 per cent solitary cysts, 62 per cent multiple and 23 per cent fluid containing cysts.

Cysts may or may not contain fluid. Those cysts which contain fluid may rupture into a bronchus. When this happens the cyst may collapse or it may be filled with air.

The wall of the cyst may have several types of lining. The lining may be greatly altered by infection. There may be no epithelial lining at all.

The cyst or cysts may be within the lung parenchyma and the structures of its wall are continuous with those of the bronchi and of the same tissue. There may be concentric smooth muscle fibers in the walls. At times cartilage is present and the cyst may be lined with ciliated stratified columnar epithelium. The cyst may be a subpleural bleb which closely resembles the subpleural bleb of emphysema. The cysts may be extraplumonary, arising apparently from rests or herniations of the bronchi or the trachea near the root of the lung.

The lining may vary. Any type of epithelial tissue may be present or as has been said before, none at all may be present. The arrangement of the elements of the cyst wall may be very irregular and the elements appear clumped together. Mucous glands may or may not be present.

Cysts may or may not be directly connected with the lumen of the bronchi. This is important. The type of connection is also important as this may be the determining factor in whether or not the cyst is symptomatic.

If a cyst contains fluid and ruptures into a bronchus it may become an air containing cyst. If a ball valve mechanism is set up so that air goes into the cyst but cannot escape, the cyst may be markedly increased in size. This is the balloon type cyst. They are usually, but not necessarily, single. The valve mechanism may not be constant so that the size may vary markedly from day to day. This is the type cyst that may cause

a sudden onset of symptoms. The smaller cysts and the fluid containing cysts usually remain unchanged unless infection is present in them. Those air cysts that are not expansile usually have a free connection with a bronchus.

Womack and Graham found evidence of a spindle cell invasion into a large number of pulmonary cysts. The lesions resembled bronchiogenic carcinoma closely, but they found no evidence of metastasis.

It is not uncommon for the larger cysts to have strands of lung tissue or bronchi passing through them. These show up in the roentgenogram as fine trabeculations traversing the cyst cavity.

Ward and Krahl described a case of cystic disease of the lung in which the cysts were lined with gastric mucosa. The cysts were not in any way connected with the gastrointestinal tract. One of the cysts communicated with a bronchus. They suggest that it was due to a pinching off of a part of the foregut in the third or fourth fetal week.

Congenital cystic disease of the lung is frequently associated with other congenital anomalies.

SYMPTOMS AND SIGNS

Most congenital lung cysts are asymptomatic. They are commonly diagnosed by some by routine x-ray or at autopsy where there has been no respiratory difficulty. The symptoms and signs associated with this condition are usually due to infection or to encroachment on the functional lung tissue by the cysts.

Cheney and Garland described a case of a 19 year old girl with a large cyst in the left lung which lowered her vital capacity to 1200 c.c. (27 per cent of normal). She danced, swam, and played tennis with no apparent discomfort. Others, however, have described cases with much less involvement in which the signs of respiratory embarrassment were very evident. This is especially true in cases in which an apparently silent cyst becomes markedly and rapidly enlarged due to a ball valve mechanism and suddenly encroaches on the surrounding lung. Such attacks may be intermittent due to changes in the type of connection with a bronchus.

As a rule, the small honeycomb cysts do not give rise to difficulty in the adult unless they are infected because there is no great or rapid change in their size. They are more likely to cause respiratory difficulty in infancy because they replace normal functional lung. If they are not extensive enough to cause decreased lung function in infancy they usually cause no distress in the adult.

There is no pathognomonic sign of cystic disease of the lung. The most commonly found signs are cough, dyspnea, wheezing, expectoration and hemoptysis. In the ball valve type of balloon cyst there may be a sudden onset of respiratory distress with cyanosis and death due to suffocation. At birth respiratory distress may be due to a lung cyst.

There may be some expectoration due to a non-infected cyst. It may be increased by changes in position.

When a cyst becomes infected fever and expectoration are usually prevalent along with the other symptoms mentioned.

In addition to the respiratory symptoms there may be marked anorexia and loss of weight, thoracic pain, vomiting and palpitation.

Physical examination findings vary with the type of cyst and the number and location of the cysts. Small cysts deep in the lung may show no signs whatever. A large tension cyst may cause a lagging of the chest on the affected side and may give a tympanitic note to percussion. The breath sounds are usually absent unless air is coming into the cyst. Fluid containing cysts, which are large, give the physical signs of any solid mass.

Kaltreider and Fray observed six patients with lung cysts. They found that in three of the cases the vital capacity and total capacity were slightly reduced and the residual air was slightly increased. The volume of the chest was increased in all cases, that is, the antero-posterior diameter was increased. There was slight carbon dioxide retention in two and slight anox-

emia in four. They found dyspnea to parallel the decrease in vital capacity.

X-ray is the most valuable diagnostic aid. Fluid containing cysts show up as areas of increased density. The air containing cysts show up as areas of decreased density with fine trabeculations. By injection of lipiodol and having the patient shift position the cavity of a cyst communicating with a bronchus may be outlined. Intracystic pressure reading may give some idea as to whether there is a patent connection with a bronchus. X-ray is not absolutely diagnostic. Exploratory thoracotomy may be the only absolute way to make the diagnosis.

DIFFERENTIAL DIAGNOSIS

Infection in a lung cyst may be mistaken for empyema. Such an error may result in prolonged treatment with poor results. Empyema with a bronchopleural fistula may even more nearly simulate an infected cyst. With empyema there is usually retraction of the chest on the affected side and there may be an approximation of the ribs. At operation the presence of a periosteal reaction with thickened ribs suggests empyema. X-ray may be of some aid. Cysts are usually spherical or oval whereas empyema is usually triangular or round and conforms to the contour of surrounding structures. There is little or no pleural thickening in cases of lung cyst. This is an important differentiation because an epithelial lined cyst will not close even though adequate drainage is effected. Biopsy of the cavity wall will determine this point.

Pneumothorax is another condition commonly mistaken for cystic disease of the lung. This is especially true of the large tension cysts. X-ray of pneumothorax shows collapse toward the hilus. This picture is altered by the presence of adhesions. As has been said before there are frequently fine trabeculations seen in cysts due to the bands of lung tissue or bronchi traversing their lumens. Cyst pressure is exerted in all directions and some lung density may be seen on all sides of the area of rarefaction. Pressure readings within the cyst or pneumothorax may be helpful but at times this procedure may be dangerous.

Herniation of the stomach or bowel into the thorax may give rise to a picture similar to cystic disease. Barium meal will rule this condition out. A large gas bubble in the stomach, especially with an elevation of the left diaphragm may be mistaken for a cystic lung at first glance.

Infected cysts may very closely resemble a lung abscess. It may be impossible to make a differential diagnosis. There may be a fluid level in both and a surrounding area of pneumonitis. Usually the cyst does not cause as much reaction, both local and general because of its epithelial lining. At times there is an epithelialization of an abscess cavity and a definite diagnosis cannot be made by biopsy. Lung abscess frequently has a history of operation in the nose or throat or aspiration of a foreign body.

At times this condition may be confused with tuberculosis. There is no positive sputum, constitutional symptoms are less, the Mantoux may not be positive in the former. Serial x-rays may be necessary to form a definite diagnosis.

Bronchiectasis may closely resemble cystic disease of the lung. Bronchiectasis is usually in the lower lobes. Schenck said many cases diagnosed bronchiectasis may very likely be in reality lung cysts. There is an overlapping of some types of each. It is frequently impossible to make a definite diagnosis when infected cysts are present.

Fluid containing cysts may resemble a dermoid cyst, echinococcus cyst, teratoma, chondroma, ganglioneuroma, and other thoracic tumors. Definite diagnosis can only be made by exploration.

Emphysema may show up in an x-ray as areas of decreased density similar to air cysts. Usually some causative factor of emphysema can be demonstrated.

TREATMENT

No set method of treatment can be given for cystic disease of the lung. The number, distribution, and size of the cysts are too inconstant to follow set rules.

Most cysts are asymptomatic and require

no treatment. In those cysts with a ball valve mechanism in which there is a rapid increase in size immediate treatment is necessary. Aspiration usually affords temporary relief. Pneumothorax is of no value because it collapses what lung is left and does not collapse the cyst. Also a pressure pneumothorax may develop. Brown and Brock used a continuous suction of the Monaldi type which collapsed the cyst and re-expanded the lung. They then made an endocutaneous flap into the cyst and connect it to the outside.

Sclerosing the bronchial opening and surgical closure of these cysts has not been very successful. Frequently it results in further stenosis without complete closure making the condition worse.

Enucleation is usually not feasible because the wall of the cyst is continuous with that of the surrounding lung.

Miller and Lillienthal inserted a one way valve through the chest wall into a cyst and got a collapse.

Collapse of a cyst will not result in permanent closure because the cysts are usually lined with epithelium.

Cauterization of the cyst wall may or may not result in closure.

Lobectomy or pneumonectomy have given the best results in the treatment of lung cysts, especially those of honeycomb type limited to one lobe or one lung and the large tension cysts.

Those cases in which the cysts are widely spread and in which operation is contraindicated must be treated conservatively. It is sometimes helpful to have such a patient move to a dry, warm climate to decrease the incidence of respiratory infection. The instillation of lipiodol has been helpful in clearing up some infected cysts.

PROGNOSIS AND COMPLICATIONS

The prognosis in congenital cysts of the lung is generally good. Most cysts are discovered accidentally or at autopsy where the patient died of some other disease.

Infection, especially in fluid containing cysts may be quite serious, especially if the extent of the disease contraindicates surgery.

Infection of a cyst is probably its most serious complication. Kirklin found tuberculous infection to be less than 5 per cent.

A sudden increase in size in a cyst may cause sudden death if treatment is not immediately instituted.

Spontaneous tension pneumothorax may result from rupture of a cyst into the pleural cavity, especially where aspiration of the cyst is attempted.

Cor pulmonale and heart failure may develop due to the increased pulmonary pressure.

SUMMARY

Congenital cystic disease of the lung is a condition which is not rare. It is very frequently asymptomatic and found at routine examination or as a casual finding at autopsy. The etiology is obscure, but most opinions are centered around faulty development of the bronchial buds. It may be confused with empyema, spontaneous pneumothorax, tuberculosis and numerous thoracic tumors. Frequently it cannot be distinguished from some cases of bronchiectasis even by the pathologist. Infection and sudden enlargement are the two most dangerous complications of the condition. There is no routine way of treating. Each case demands treatment according to its type. Inoperable cases may be helped by moving to a dry climate to reduce the incidence of respiratory infections.

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THE BONE MARROW IN DISEASES OF THE LEUKOPOIETIC SYSTEM

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HISTORY

Until seventy years ago bone marrow was an unexplored tissue. It is only within the last 35 years that the bone marrow has been employed during life as a means of diagnosis. Ghedini, in 1908, reported the first study on the subject when he biopsied the tibia and demonstrated the presence of parasites in cases of malaria and leishmaniasis. Seyfaith, in 1923, improved on this by selecting the sternum as the site of biopsy, because the sternal marrow was more active throughout life and was more accessible. Then, in 1927, Arinkin introduced the aspiration method which has been very widely used and added greatly to the knowledge of the cytology of bone marrow!

PURPOSE OF PAPER

It is the purpose of this paper: (1) to familiarize the reader with the origin and morphology of the cells of the normal bone marrow; (2) to give in a detailed manner the technic of sternal puncture and in a generalized manner other less widely used methods of bone marrow study; (3) to give the clinical indications for sternal biopsy; (4) to inform the reader what conditions produce marrow changes which are specific; and (5) to aid the reader in establishing a diagnosis of the more important leukopoietic diseases by bone marrow examination.

For reasons to be presented later the biopsied material here described was obtained by the sternal puncture method.

NORMAL MYELOGRAM

In order for one intelligently to study the bone marrow in pathologic states, a working knowledge of the normal marrow is practically indispensable for proper interpretation. Schilling coined the name haemogram to designate the qualitative blood picture; likewise the term myelogram can reasonably be applied to the marrow picture.

Origin of Cells: There are two trains of thought concerning the origin of blood cells during postnatal life. One group (the monophyletic school) contends that the cells of the blood are derived from a single primitive stem cell, whereas the other group (the polyphyletic school) contends that the various blood cells have individual precursors and separate cycles of maturation.

Notable figures such as Pappenheim, Maximow, and Downey are of the monophyletic school and adhere to the idea that a single polyvalent cell, the "lymphoidocyte" or hematocytoblast is present in all adult hematopoietic tissues and this cell gives rise to the other cells of the blood.

The polyphyletists, on the other hand, deny any such cell as the hematocytoblast but differ among themselves concerning the number of leukoblastic stem cells: the dualists contending that there are two stem

cells, lymphoblast and myeloblast; and the trialist contending there are three stem cells, lymphoblast, myeloblast and monoblast. The latter is the most widely accepted theory. It not only postulates an individual stem cell for every type of blood cell, but advocates a different site of origin in normal postnatal life.

Cytology: As has been mentioned, it is absolutely essential that one have a working knowledge of the cells in the normal marrow in order to recognize the marrow in pathologic states. It is evident that there is still much diversity of opinion as to the stem cells of the various cell series. There are also considerable variations as to the appearance of the normal marrow. This has led some workers (Propp and Schwind[4]) arbitrarily to grade the cellularity of the marrows in their series into four groups or grades. Grade 1 marrows have approximately the number of nucleated cells found in peripheral blood smears. Grade 2 marrows have four to five times this number of cells, and Grade 3 marrows have from ten to twenty times this number. In Grade 4 marrows there are more nucleated cells than erythrocytes, and the cells appear on the smears in clumps and masses. According to these workers, Grade 2 is the most common. Grade 4 type occurs only in abnormal conditions where the marrow is extremely hyperplastic.

In studying marrow films, several points should be kept in mind.[5] Marrow films, unlike blood, have a semi-solid matrix background in which lie parts of cells, naked nuclei and cell granules. In determining the percentages of the various cell types in marrow films, a larger number of cells should be counted than is customary in blood counts, because there are usually more cells and they are far from being evenly distributed. Piney[5] says that at least one thousand cells should be examined, preferable in several films. The relative proportions of red and white cells must be determined as in the blood, but in comparing them with the differential count of the peripheral blood separate myelograms of the white cells should be obtained.

In order to avoid any further confusion regarding the cytology of bone marrow, I have selected Piney's description of the various cellular elements of the normal marrow.[5]

Since all cells, regardless of type, are thought to originate from some stem cell belonging to the reticulo-endothelial system, the haemohistioblast (one of its members) has been described by Ferrata as being the stem cell. It is so primitive and undifferentiated that it is capable of developing into connective tissue or into blood. These cells are about fifteen to twenty microns in diameter with a delicate, irregular, slightly basophilic cytoplasm. The mucleus is round or oval, of fine, delicately reticulated structure in which one or more distinctive nucleoli are found. Recognition in marrow films is by the nuclei, since the cytoplasm is so delicate that it usually ruptures.

The nature of the hematocytoblast is still not definitely determined. Suffice it to say that it is smaller in size and more definite in shape than the more primitive haemohistioblast. The cytoplasm is devoid of granules, distinctly basophilic, and varies considerably in amount. The nucleus is denser than that of the haemohistioblast having interlacing fibrils of basi-chromatin in which one or more nucleoli are present.

The myeloblast, although very difficult to distinguish from the hematocytoblast, has a nucleus which is less dense and cytoplasm which is less basophilic. In any case, definite differentiation is practically impossible.

The premyelocyte is an intermediate cell type between the myeloblast and the myelocyte, and there is no doubt as to its myeloid nature. The nucleus is denser and more deeply stained than that of the myeloblast, but nucleoli can still be detected in it. The cytoplasm is homogenous and less basophilic than that of the myeloblast.

Two grades of premyelocytes are described: those having immature, azurophilic granules; and those having granules of the same tinctorial properties as mature cells. The former have nucleoli resembling those

of myeloblasts, whereas the latter have a denser structure.

As with the more mature forms, three varieties of immature premyelocytes are described: those with minute azurophilic granules, all the same size—preneutrophilic premyelocytes; those with larger rather scanty azurophilic granules, all the same size—pre-eosinophilic premyelocytes; and those with large irregular azurophilic granules, of different sizes—pre-basophilic premyelocytes. These, by maturation, give rise to premyelocytes with their respective types of granulation; and these in turn give rise to myelocytes.

Myelocytes vary greatly in size (10-25 microns). The nucleus is circular, but the edge may appear to be indented by the granules that fill the cytoplasm. The basi-chromatin has still a detectable reticular arrangement, but condensations may also be seen. The cytoplasm is fairly basophilic, but almost obscured by granules which have attained their definite character—neutrophilic, eosinophilic, or basophilic.

Metamyelocytes represent an intermediate stage between myelocytes and mature polymorphonuclears. Schilling has divided these into two groups: juvenile forms which have a slight indentation of the nucleus; and staff forms with deeply indented, but not lobulated, nuclei. The nuclei of the eosinophiles are more difficult to recognize, because they are pale and covered by large granules. The nuclei of the basophiles are even less distinct, and frequently it is impossible to recognize the two types of metamyelocytes.

The polymorphonuclears as seen in marraw films are identical in character with those found in the peripheral blood; and a description of their structure is not deemed necessary here.

Lymphocytes, although in a sense not constituents of the normal marrow, are found in small numbers. They occur only in groups, sometimes even with a germ-center. There is some evidence that suggests that the marrow may, in a small way, be a site for the production of lymphocytes since the marrow contains more large lymphocytes than does the blood.

The small lymphocytes of the marrow resemble those found in the peripheral blood; and the large forms differ from the small forms only in the amount of cytoplasm they contain; the nuclear characters are the same.

During health few, if any, immature cells of the lymphocytic series are found in the marrow. The lymphoblast is the early cell form from which the lymphocytes arise; and it is irreversibly determined in the direction of lymphocytopoiesis. Its structure is about the same as the myeloblast, but the nucleus is relatively larger and occupies most of the cell. It is reticulated rather more coarsely than that of the myeloblast, and contains nucleoli, around which the basi-chromatin is slightly condensed.

Monocytes are scanty in normal marrow and are identical with those found in the peripheral blood.

Plasma cells, although scanty, are normal constituents of the marrow. The cells are large (15-20 microns), have an eccentric nucleus with the basi-chromatin arranged in a radial pattern. The cytoplasm is intensely basophilic throughout, except for a peri-nuclear pallor.

Turk cells are very similar to plasma cells except the nucleus is not eccentric. In fact, some workers contend that they are the same cell—the turk cell being an immature form of the plasma cell. These, like plasma cells, are also scanty in the normal marrow.

Megakaryocytes are fairly numerous and important constituents of the normal marrow. These vary from 30-90 microns in diameter; and have a very faintly basophilic cytoplasm in which groups of minute azurophilic granules are present, especially near the periphery. The nuclei are whorled and lobulated in a most complicated manner; basi-chromatin occurs in large masses without any definite distribution. Complete cells are rarely found in marrow films, and the recognition of the fragments present is very difficult.

Since the scope of this paper is confined to the leukopoietic system, the appearances of the various hemoglobiniferous elements need not be described. Suffice it to say that the normoblastic series begins with the hematocytoblastic stage, as do other blood cells, and ends with the development of the ordinary red corpuscles.

As the normal marrow varies in other respects, so do the percentages of the different cells vary. This may be actual or may be due to inevitable errors. According to Piney, the following table gives the normal variations.

	Per cent
Neutrophiles:	
Myelocytes	30-35
Metamyelocytes	10-15
Polymorphs	24-30
Eosinophiles	
Myelocytes	1-2
Polymorphs	½-1
Basophiles:	
Myelocytes	3-6
Polymorphs	1-2
Premyelocytes	1-2
Hematocytoblasts, including myeloblasts	1-2
Haemohistioblasts	¼-½
Lymphocytes:	
Small	6-9
Large	8-12
Plasma cells	½-1
Pro-erythroblasts	1-2
Normoblasts	15-20
Megaloblasts	2-3
Megakaryocytes	scanty, but invariable

BONE MARROW BIOPSY

1. Trephine methods:[6] This method was first introduced by Pianese (in 1903) who obtained marrow for examination by trephining the femur. At present, however, the sternum is the site of choice. Even though this is an operating room procedure and is not the most widely used method, it is considered by Custer[6] and other workers to be the method of choice.

The procedure is essentially that of obtaining a button of bone with a 1 cm. diameter trephine from the ventral surface of the sternum, fixing it in Helly's fluid, decalcifying, embedding the specimen in paraffin, and then sectioning the specimen from its deep surface. The sections should then be stained with Maximow's Azure II eosin method. Fragments of marrow may be curetted from the margin of the cavity in the bone, pressed against, and drawn across clean micro slides and stained. Tissue cultures and supravital preparations may be made when indicated.

It must be remembered that dry imprints should be examined along with sections, because intrinsic cellular detail is clearer, blood smear comparisons are possible, and a correlation between the peripheral blood picture and marrow picture can be obtained.

2. *Aspiration method:*[4] This method of bone marrow examination is more widely used than any other because of its simplicity, but the novice should be forewarned of the technic, because his first attempts are apt to be unsatisfactory.

This technic consists in using 18 gauge spinal type needles with a heavy finger tip and stylet. Needles are cut in 2, 1.5 and 1 cm. lengths, and are used depending upon the size of the individual. Puncture is made in the midline of the body of the sternum at the level of the third costosternal synchrondrosis. Other levels may be used, if this site is not available, or if a check is desired. Probably in children, it is better to make the puncture at the level of the third interspace, because not infrequently the first and second sternebrae dot not unite until adult life is reached. One must maintain strict surgical asepsis. The skin, subcutaneous tissue, and periosteum are infiltrated with a total of about 3 c.c. of novacaine. This will usually produce the desired amount of anesthesia. The puncture needle is inserted vertically, and, finally, the outer table of the sternum is pierced by a rotary movement of the needle under firm pressure. Boring is continued until the needle becomes fixed in the bone. The stylet is removed and a tuberculin syringe or large syringe, if necessary, is attached and suction exerted by pulling on the plunger. If no marrow appears, the needle is

advanced farther and aspiration is tried again. This is continued until the appearance of gross blood at the distal end of the syringe. This should be about 0.2 c.c. Suction should then be stopped, and the needle and syringe withdrawn. Care should be taken to hold the syringe with its attached needle horizontally to prevent extrusion of drops of marrow from the end of the needle.

Very little pain is produced in performing a sternal puncture. Occasionally, however, some pain is produced when the periosteum is pierced by the infiltrating needle, and one may experience a not severe aching in the chest. This is transitory however, and is probably due to the temporary negative pressure in the marrow cavity. After the needle is withdrawn, a sterile compress is applied to the puncture wound and held in place with adhesive for 48 hours.

It has been found that the most satisfactory portion for study is that which enters the needle last, and, therefore is used for making the first smears. Anticoagulants are to be avoided, because they interfere with staining. Therefore, one must work rapidly since clotting occurs quickly in the needle. The needle and syringe are held horizontally with the opening of the needle face down, and small drops of marrow are made to appear at the opening by pressure on the plunger. The drops should be small, and at least twelve dried smears are made on clean cover slips. The cells on the smears should lie close together but not overlap. Smears that are too thick do not stain well; if too thin, the more fragile cells will break up. If smears are not dried quickly, they will not stain properly. Either Wright's stain or the May-Gruenwald-Giemsa stain may be used. The former is by far the easier and more widely used of these stains.

Reticulocyte counts, for the sake of uniformity, are made from the second drop of marrow coming from the needle. The material is smeared on a slide and stained according to the brilliant cresyl blue technic.

Although supravital preparations are made with every puncture by some workers, they are not an essential part of the technic but may be of value in the identification of monocytes.

3. *Comparative value of methods presented:*[6, 7] Even though bone marrow studies of the hematopoietic system are relatively recent, their value cannot be overestimated. By employing the trephine method, one can determine the state of hyperactivity, hypoplasia or defective maturation in one or all of the cell series; whereas in aspirated marrow these matters are questionable, because the cells do not retain their original relationship, probably not their relative proportions, and the material withdrawn is apt not to be representative. Focal lesions of diagnostic value are very apt to be missed, and aspirative marrow is often unavoidably diluted with blood. Lastly, the cells are subjected to more trauma and are more likely to be damaged in preparing marrow-blood mixtures, whereas in sections they are well preserved.

The aspiration method is more widely used because of its simplicity, and repeated biopsies on the same individual may be performed. It is also quite satisfactory in certain instances, since it enables one to make a diagnosis without employing the more radical procedure of trephining. One should employ both procedures if necessary, using the trephine method only when the more conservative aspiration method fails to give the desired information.

4. *Drill method:*[6] Favorite compromised between the methods mentioned above and devised a drill method. This consisted of a drill ensheathed by a cannula. After introducing the drill into the marrow cavity, it is rotated and fragments are withdrawn from which imprints and sections can be made. By retaining the cannula in place, one can introduce the drill at different angles thereby obtaining more material and examining a larger area.

CLINICAL INDICATIONS FOR BIOPSY

The question arises, when is the sternal puncture method of marrow biopsy indicated? According to Propp and Schwind,[4] it should always be performed when: (1)

the diagnosis is in doubt, and a disease usually showing a typical myelogram cannot be excluded; (2) the etiology of the peripheral blood is obscure; (3) other means of biopsy have failed. It may be done: (1) to save time, if a specific marrow picture is likely to be present; (2) to obtain information concerning prognosis; (3) to determine response to treatment; (4) to determine the type of "stem cell" leukemia when this cannot be done from the peripheral blood. It should also be performed whenever splenomegaly is present.

MYELOGRAM CHANGES IN LEUKOPOIETIC DISEASES

A. *Specific and non-specific myelograms:*[4] Sternal puncture findings fall into two categories, specific and non-specific. Myelograms which are typical of a particular disease, and which when present are so reliable as either to indicate the diagnosis or to be actually pathognomonic, are termed specific or typical myelograms. These are found in the following conditions: (1) leukemia, especially acute and leukopenic leukemia; (2) megaloblastic marrow, present typically in pernicious anemia in relapse, achrestic anemia, and sprue; (3) agranulocytosis in the arrested marrow stage; (4) neoplasms: multiple myeloma and metastatic malignancies, especially carcinoma; (5) lipoid histiocytosis; (6) malaria, and (7) leishmaniasis (kala-azar).

It should be remembered that the above conditions will not always give diagnostic marrow pictures, but when specific findings are present, they do indicate the diagnosis. Bizarre cases may be encountered which confuse the picture very much. The absence of a typical myelogram cannot be relied upon to rule out a disease in differential diagnosis, because of the possibility of an error in sampling or atypical variations in pathology. But negative findings may be extremely useful in some instances.

All other diseases so far studied constitute the non-specific group. Although the myelograms in this group are non-typical, they are often of great interest and usefulness in relation to the general clinical picture.

B. *Pathological states:*

1. Leukemias: Even though the bone marrow picture in the various forms of leukemia are rather complex, they are more clearly defined than any other disease entity affecting the hematopoietic system. Frequently it is possible to make a diagnosis clinically employing the ordinary blood examination to confirm it, discover the type and give some indication of the severity of the disease. But the marrow examination reveals a much clearer insight to the severity, changes indicative of approaching relapse and valuable information concerning therapeutic control.

a. Chronic myeloid leukemia:[5] Marrow examination is not of much value in the early stages of this condition, because slight changes in the marrow are difficult to recognize, as has been mentioned.

During health, mature polymorphs are thought to be formed by division and maturation of myelocytes and development from the less mature types, such as the myeloblast plays little, if any, role in granulopoiesis after birth. Likewise, the normal mechanism persists to a considerable degree in chronic myeloid leukemia.

When definite changes in the bone marrow have developed, one finds a marked increase in the cellularity. This increase consists mainly of myelocytes which may, in some cases, constitute as much as 80 per cent of the white cells present. Most of the white cells are neutrophiles, but eosinophiles and basophiles are also increased. Some myelocytes contain both eosinophilic and basophilic granules. The cells are larger and less mature than the corresponding cells found in peripheral blood. The following table shows a fairly typical myelogram in a case of chronic myeloid leukemia.

Total Nucleated cells 70,000 but variable

	Per cent
Myeloblasts	1.1
Promyelocytes	0
Myelocytes	37.4
Nonsegmented neutrophiles	31.0
Segmented neutrophiles	20.0
Eosinophilic myelocytes	5.6
Nonsegmented eosinophiles	0

Eosinophiles	3.4
Lymphocytes	0
Monocytes	0
Megaloblasts	2.0
Normoblasts	2.2
Megakaryocytes	0.2

Two other important but difficult points to determine are: (1) the background of the film (matrix) in chronic myeloid leukemia is denser and contains more granules and debris than is found in normal healthy marrow, and (2) the cells (or some of them) tend to lie in groups which are all composed of a single cell type. Mitotic figures are most frequently seen in these cell groups, and if such is the case with myeloblasts, it is suggested that the morbid process is becoming more active.

Patients with leukemia should have sternal punctures performed periodically, and when there is a great increase in the number of cells less differentiated than myelocytes, it is indicative of an eminent relapse, of an acute exacerbation. One can thus be forewarned of such changes, since changes in the bone marrow precede the changes in the peripheral blood.

It is important to examine the marrow very carefully in the early stages, since it is extremely easy to mistake the appearance of the marrow for that of a simple reactive hyperplasia, such as may be associated with any infection, because in chronic myeloid leukemia there are, in addition to the leukoblastic changes, erythroblastic and megakaryocytic reactions.

b. Chronic lymphatic leukemia:[5] In this condition the myelogram is usually easy to interpret, since lymphocytes are not numerous in the normal marrow, and never show signs of activity. The lymphocytes are very closely packed together, but may be interrupted in various places by small nests of red cells and granulocytes. The background of the film is moderately thick, but hyaline, and unlike that seen in chronic myeloid leukemia.

Small lymphocytes, with a variable proportion of large forms, constitute most of the cells. Cells of the lymphoblastic group are usually scarce. An increase in cells of this series implies active progress of the disease. If lymphoblasts are very numerous, the prognosis is grave, and in all probability radiotherapy will only aggravate the condition. In early cases, if the focal arrangement of lymphocytes is present, it is pathognomonic of the condition.

Although sternal puncture is rarely needed to diagnose chronic myeloid leukemia, it may be of utmost value in the diagnosis of chronic lymphatic leukemia, because atypical forms are quite common. This is especially true of chronic aleukemic leukemia which may be without any of the classical signs of leukemia (see aleukemic leukemia).

The myelogram in a typical fairly advanced case of chronic lymphatic leukemia is shown in table below.

Neutrophiles:	Per cent
Myelocytes	1-2
Metamyelocytes	1-2
Polymorphs	1-2
Eosinophiles	0-8
Lymphocytes:	
Small	30-40
Large	30-40
Immature	10-20
Blasts	5-15
Monocytes	2-5
Normoblasts	2-5
Megakaryocytes	2-4

c. Monocytic leukemia:[5] The exact nature of this condition is still uncertain, probably because it is a relatively uncommon type of leukemia. Most of these cases tend to be acute or subacute rather than chronic. Aside from this characteristic there is no clinical difference between monocytic leukemia and the other types of leukemia.

There is in this condition a massive proliferation of the cells of the reticuloendothelial system. This takes place to such an extent in the bone marrow, that the normal myeloid tissue becomes ultimately excluded. There is both a relative and absolute increase in the monocytic type of cells. These may form as much as 95 per cent of the total leukocytes. Most of the cells are of the classical kind, large, but varying

in size. Younger forms may be found but are usually present in smaller numbers.

The fact that the immature elements are more numerous than fully differentiated ones, conforms with the knowledge that this condition is generally more rapid in its evolution.

In this condition the peripheral blood shows an increase in the number of white cells up to 400,000 per cu. mm. But here again aleukemia cases occur, and unless myelograms are studied, the diagnosis may be missed (see aleukemic leukemia). Although monocytes make up most of the cells ordinarily, the terminal stages are manifested by a marked increase in the monoblasts. Again, as was mentioned before, the changes in the bone marrow precede those in the peripheral blood, and for obvious reasons marrow examinations should be performed.

d. Acute leukemia:[5] This condition may be primary or it may be the terminal phase of a chronic case. The myelograms in these conditions are varied and might lead one to suppose that there is an infinite number of types of acute leukemia. Although in some cases the acute forms may be differentiated into myeloid, lymphatic and monocytic forms, there are many instances where the cells infiltrating the marrow are so undifferentiated and primitive that it is practically impossible to ascertain their nature. Such a condition can simply be termed acute leukoblastosis or acute leukemia. Piney has said, "all cases of acute leukemia are hematologically and, sometimes, clinically atypical." Other workers, on the other hand, say that in their series the marrow was invariably typical. These workers found that the normal cells were almost entirely replaced by lymphoblasts and lymphocytes in the acute lymphatic type, and by myeloblasts and myelocytes in the acute myeloid type. In all their cases of acute involvement, there was a marked diminution in the erythroid and megakaryocytic elements.

The monocytic variety may be differentiated from other types of acute leukemia by employing the peroxidase staining technic in much the same way that is employed in the peripheral blood examination.

The acute type of monocytic differs from the chronic type only in that the cells retain their fixed position in relation to the reticular fibrillae, whereas, in the chronic they become rounded up and free, often phagocytosing erythrocytes and debris.

e. Plasma cell leukemia:[6] In this condition, there is marked dissemination of plasmoblasts and plasmocytes throughout the myeloid cavities. These are more readily recognized from the characteristic morphology of the more mature forms. This can be differentiated from plasma cell myeloma by its diffuse type of proliferation and the absence of osteopysis.

f. Megakaryocytic leukemia:[6] There is much dispute that this condition exists as a separate entity. Little more needs to be said except that many workers have found it almost impossible to differentiate this condition from cases of chronic myelosis in which there is extensive megakaryocytic proliferation.

g. Aleukemic leukemia:[8] Diagnosis in this condition may be impossible, since the total leukocyte count of the peripheral blood may be normal or subnormal. Occasionally, however, a few immature leukocytes may be found in the peripheral blood but nothing diagnostic like one finds in the bone marrow. It has been estimated that 10 per cent or more of all leukemic cases are of this type.

It is the belief of most workers that this condition is just a stage in the leukemic process. Both acute and chronic forms occur, and all of the various types, myelogenous, lymphogenous and monocytic, have been described.

The clinical picture is essentially the same as that seen in the more typical forms of the various leukemias, except for the peripheral blood picture changes. The diagnosis depends upon the bone marrow picture which will show the typical myelogram changes which were discussed under the ordinary types of leukemia; of course, the findings will depend upon the type of leukemia present. Obviously, in these condi-

tions it is very important that the marrow pictures be compared with the peripheral blood pictures.

2. Leukemoid reactions: Such reactions are of value here, because they are characterized by blood changes which resemble those of leukemia and must be ruled out in the differential diagnosis. The diagnosis based upon blood and marrow examinations is difficult because of the varied reacting power of the bone marrow; but even the possible types of reactions are limited. The difficulty in differentiation from leukemia is dependent upon whether the marrow reaction affects the erythrocytopoietic tissue mainly; in which instance the problem is less difficult than when the leukoblastic cells are involved, where differentiation is almost impossible. According to Piney, blood examination is more important for diagnosis than bone marrow examination in leukemoid reactions.

Krumbhaar[9] divided leukemoid reactions into two groups: (1) those presenting signs and symptoms suggestive of leukemia, and (2) those that resemble leukemia only from the hematological standpoint. Many and varied causes may produce leukemoid reactions, and it has been stated that all cases of supposedly leukemias which have recovered were none other than another type of leukemoid reaction. The bone marrow picture is, generally speaking, similar to that present in the peripheral blood. Hill and Duncan[10] have drawn up the following table which is very helpful in the laboratory differential diagnosis between true leukemias and leukemoid reactions:

True leukemias	Leukemoid reactions
1. Leukocytes are atypical, particularly the immature ones.	1. Immature as well as mature leukocytes show normal morphology.
2. Myeloblasts may be numerous, as high as 99 per cent.	2. Myeloblasts usually less than 10 per cent.
3. Immature erythrocytes are rarely increased in proportion to the increase of immature leukocytes.	3. Erythroblasts often increase in proportion to immature leukocytes.
4. Platelets are decreased often severely; may be increased only in chronic myelocytic leukemia.	4. Platelets are usually normal or increased but may be moderately decreased.
5. Progressive anemia which may become worse.	5. Anemia is variable depending upon the cause.

3. Essential thrombocytopenic purpura:[11] Mature megakaryocytes are formed from myeloblasts through a process called homoplastic hemopoiesis. Thus any disturbance which involves the stem cell (myeloblast) will ultimately interfere with the normal development of the megakaryocyte, thereby resulting in a qualitative and quantitative change in them. Since all this takes place in the bone marrow, examination of it represents the most important single differential diagnostic features.

In acute thrombocytopenic purpura, the myelogram reveals a uniform stimulation with a myeloid, erythroid, and most important of all, a megakaryocytic hyperplasia. In the more chronic stages, without hemorrhages, the myeloid and erythroid hyperplasia may be absent, but the megakaryocytic hyperplasia persists. In the acute phase of the disease, many of the megakaryocytes are young forms, whereas, in the more chronic phases, the megakaryocytes are adult in type and possess an abundance of azurophilic granules in their cytoplasm. Some of the megakaryocytes reveal hyaline changes in their cytoplasm, and the azurophilic granules may be absent. Degenerated or toxic forms with vacuolization of their cytoplasm are occasionally seen, but are more frequently seen in larger numbers in some cases of symptomatic purpura hemorrhagica, especially those due to infections and intoxications.

4. Agranulocytosis:[12] There has been much discussion concerning the etiology of agranulocytosis. In all cases where the etiology is in question, sternal marrow studies should be performed, because they may be of value in revealing the underlying cause, such as, leukosis or panmyelophthisis.

The bone marrow picture in this condition shows marked variations. These may be grouped into three types: (1) aplastic, (2) normal or hyperplastic, and (3) reticulo-endothelial.

a. Aplastic: The aplasia involves the granulocytes and myeloblasts. The megakaryocytes and erythrocytes are usually very little affected. The marrow picture shows infiltration throughout with lymphocytes and plasma cells. The aplasia may be partial or there may be complete absence

of polymorphonuclear cells. When there is marked leukopenia with the complete absence of polymorphonuclear cells the prognosis is grave.

b. Normal or hyperplastic: In this type the marrow picture shows many myeloblasts and a few myelocytes, although the granulocytes are completely absent from the peripheral blood. Normal or hyperplastic marrows are often found in cases during remissions and in cases which have recovered. The finding of such a marrow picture therefore is usually indicative of a favorable prognosis.

c. Reticulo-endothelial: In this type, only a few myeloblasts and myelocytes are seen in the bone marrow. Otherwise, it resembles the aplastic type, except for the marked hyperplasia of the reticulo-endothelial system. The reticulo-endothelial cells may assume various forms; they may appear as foam cells or clasmatocytes or may assume phagocytic proportions.

5. Infectious mononucleosis:[13] There has been much dispute concerning the sternal marrow findings in this condition. However, it is the opinion of most authors that there is little or no change in the sternal marrow beyond a moderate shift to the left of granulopoiesis. Other workers, such as Freeman (1936), Markoff (1936), and Mallanue (1937), on the other hand, have all found an increase in the cells of the lymphocytic series. Scott (1939), however, seems to think that the findings of the above three workers were due to dilution with the peripheral blood. He says that sternal puncture is of very little value in diagnosing infectious mononucleosis, because even finding a normal marrow, which often occurs, does not exclude lymphoid leukosis.

6. Leukopenic states:[2] Normally neutrophiles are produced in the bone marrow and released in sufficient numbers to maintain the normal number in the peripheral blood. If there be a deficiency of the hypothetical maturation factor or the factor which regulates the release of mature cells into the blood, or if some toxic agent destroys the neutrophiles in the peripheral blood, a leukopenic condition will be present.

Bone marrow studies indicate that in the leukopenic states, the marrow fails to produce a sufficient number of cells rather than their increased destruction in the peripheral blood. If the marrow is subjected to depressing influences, cell development may be altered so that development occurs at a less mature level, or there may be a decrease in the number of mature cells producing the mature types, even though there is no arrest of normal maturation.

Leukopenia may be due to many different conditions, however, it is not the scope of this paper to elaborate on the bone marrow findings in all the conditions producing leukopenia, except to say that in those instances where the primary effect is on the bone marrow, the myelogram reveals a depression of granulopoiesis.

7. Protozoal diseases:[5]

a. Kala-azar: The myelogram in this condition is specific. The marrow is hyperplastic. There is a marked increase in lymphocytes, intense reticulo-endothelial hyperplasia, patchy distribution of platelets, and a marked increase in monocytes in which are found the Leishmania. These consist of a tenuous membrane surrounding a cytoplasm which is faintly basophilic in character, in which minute inclusion bodies are found. These bodies consist of a nucleus which is large and stains deep violet, and centrosomes which are smaller, rod-shaped, and stain moderately basophilic.

Even though the leishmania may be absent in the bone marrow, the myelogram is characteristic. The following table, according to Piney, is a representative myelogram in this condition:

	Per cent
Neutrophiles:	
Myelocytes	18-24
Metamyelocytes	0-1
Polymorphs	8-10
Eosinophiles	0-1
Lymphocytes:	
Small	18-22
Large	18-22
Monocytes	14-18
Plasma cells	1-3

Haemohistioblasts	0-1
Hematocytoblasts	0-1
Normoblasts	3-5
Megaloblasts	1-3

Films show increased cellularity; and platelets are increased.

b. Malaria: Finding the parasites in the marrow cells is not common, but when they are found they are specific. Essentially the marrow findings are monocytic and normoblastic. The monocytic response is more marked in chronic cases than in acute ones. The following table gives a fairly representative picture of the bone marrow in this condition:

Neutrophiles:	Per cent
Myelocytes	5-7
Metamyelocytes	0-2
Polymorphs	9-12
Eosinophiles	0-2
Monocytes	10-14
Lymphocytes	2-3
Premyelocytes	0-2
Hematocytoblasts	0-1
Normoblasts	40-50
Macronormoblasts	12-16

8. Tumors:

a. Multiple myeloma:[5] This is the most common type of primary tumor. Although the sternal bone marrow findings are variable, the presence of the so-called "myeloma cells" which make up 3 to 65 per cent of all the cells, is pathognomonic of the condition. The absence of these cells, however, does not rule it out. Even though diagnosis is possible by clinical and radiological methods, changes in the bone marrow take place before peripheral blood changes or clinical and radiological evidence is present.

Most of the cells are of the plasmocytic variety, but myelocytic and erythroblastic responses, though rare, do occur.

There has been much dispute concerning the nature of the "myeloma cell", but whatever the nature of this cell, it appears as a large round or ovoid cell about 15 to 30 microns in diameter. The diameter of the nucleus is from 5 to 7 microns, usually eccentric in position, occasionally nucleolated and leptochromatic, but more often stains densely. Cartwheel arrangements are uncommon. The cytoplasm is basophilic and a pale perinuclear zone may be present; cytoplasmic vacuoles are frequently present. At times 2 or 3 nuclei may be present, but mitotic figures are not seen.

b. Chloroma:[5] The position of this tumor-like condition is far from being clear. Suffice it to say that the bone marrow picture presents the appearance of a leukemia (usually the myeloblastic type) and differs from it through the formation of intra and extra medullary tumor masses. There is a marked tendency for these tumors to invade or erode adjacent structures.

c. Hodgkin's disease:[13] There has been much diversity of opinion among workers in this condition. Most of the authors state that there is no change in the bone marrow beyond a shift to the left of a granulopoiesis with occasional toxic changes. Some workers, Rohr and Hegglin (1936), and Varadi (1938), claim they have found Reed-Sternberg cells in the puncture films, but this has also been disputed by others workers; diagnosis, as before, depends upon the histiological study of an excised lymph node.

d. Storage diseases:[2] The so-called lipoid and non-lipoid histiocytoses (which include Niemann - Pick, Hand - Schüller - Christian, Gaucher) are all really more generalized diseases, but affect the reticulo-endothelial elements of the bone marrow, spleen, as well as other organs, and may produce local areas of myelophthisis and bone rarefaction. The presence of extremely large, mononucleated cells with or without lipoid material in their cytoplasm is diagnostic according to type. Bone marrow biopsies are mainly helpful in confirming rather than making a diagnosis in these conditions.

e. Ewing's tumor:[5] This is a very good example of a tumor that arises from the reticulo-endothelial system of the bone marrow. In the early stages sternal puncture will reveal a normal myelogram, but metastasis from its usual primary focus in the long bones is widespread; and long before there is either clinical or radiological evidence of metastasis, the sternal marrow may contain scattered tumor cells. These cells are large with indented nuclei, irreg-

ular hyaline cytoplasm, and resemble histiocytes, possessing all of the characteristics of what are sometimes called dismorphocaryocytes.

Much investigation and study is needed on the reticulo-sarcomas and their allied conditions. With the present knowledge one can make a diagnosis of malignancy or of innocence, but very little can be said about their origin.

f. Secondary tumors:[5] These tumors are much more common than primary growths. It is surprising how frequent tumor cells and signs of hypoplasia can be detected in the absence of clinical and radiological findings. Metastatic tumor cells differ considerably from those found in their primary growth site. In the marrow they are almost always found in groups composed of small and large cells, with a tendency to become much more elongated than epithelial cells elsewhere. Therefore, it is very difficult to determine where the primary site of the tumor is situated.

The myeloid tissue is usually extremely active, thus accounting for the leuko-erthroblastic anemia that may accompany marrow metastasis. But aplasia may occur, and this is often associated with some osteosclerosis.

It is evident that the use of this procedure routinely would indicate that many clinically operable cases have already passed the stage in which cure is possible.

SUMMARY

1. A brief history of bone marrow biopsy has been given.

2. The appearance of the normal myelogram has been described in detail.

3. Three methods of bone marrow biopsy now employed were described: (a) trephine method; (b) aspiration method, and (c) drill method.

By employing the trephine method, one can determine the state of hyperactivity, hypoplasia or defective maturation in one or all of the cell series; whereas in aspirated marrow these matters are questionable, because the cells do not retain their original relationship, probably not their relative proportions, and the material withdrawn is apt not to be representative. Focal lesions are apt to be missed, and aspirated marrow is often unavoidably diluted with blood. Lastly, the cells are more likely to be damaged in preparing blood-marrow mixtures.

However, the aspiration method is simpler, more widely used and repeated biopsies on the same individual may be performed. It is quite satisfactory in certain instances where one does not want to employ the more radical operative procedure of trephining. One should employ both procedures, if necessary, using the trephine method when the more conservative aspiration method fails to give the desired information. The drill method was devised in an attempt to combine the virtues of the trephine and aspiration methods, but as yet is not used very much.

4. Sternal puncture is indicated when: (a) the diagnosis is in doubt and a disease usually showing a typical myelogram cannot be excluded; (b) the etiology of the peripheral blood is obscure; (c) other means of biopsy have failed. It may be also done: (a) to save time if a specific marrow picture is likely to be present; (b) to obtain information concerning prognosis; (c) to determine response to treatment, and (d) determine type of "stem cell" leukemia when this cannot be done from the peripheral blood. It should also be performed whenever splenomegaly is present.

5. The myelogram changes in the more important leukopoietic diseases have been presented with special mention being made of those conditions which produce typical myelograms. Typical myelograms are found in: (a) leukemia, especially acute and aleukemic leukemia; (b) megaloblastic marrow, present typically in pernicious anemia in relapse, achrestic anemia, and sprue; (c) agranulocytosis in the arrested marrow stage; (d) neoplasms: multiple myeloma and metastatic malignancies, especially carcinoma; (e) lipoid histiocytosis; (f) malaria, and (g) leishmaniasis (kala-azar).

CONCLUSIONS

1. Taking all things into consideration, the aspiration method of sternal bone mar-

row biopsy has been found to be the most practical and widely used.

2. Sternal puncture has provided the hematologist with a relatively new and valuable diagnostic procedure which should be employed when it is indicated. It should, however, not be used alone, but in conjunction with other clinical and laboratory data to establish and confirm a diagnosis.

3. One of the greatest handicaps with bone marrow studies is that too few workers are adequately trained to study and recognize intelligently all of the various types of cells found in the bone marrow.

4. Finally, the study and diagnosis of diseases by sternal marrow biopsy is still a relatively new field, and much investigation is needed along these lines before myelogram examination becomes an art.

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THE WAGNER-MURRAY-DINGELL BILLS

These bills, the one introduced in the Senate by Senators Wagner and Murray and a similar one in the House by Representative Dingell, according to newspaper columnists and other press and radio information, seem to have lost considerable amount of support from several of the important groups that were originally very enthusiastic about them. Labor, for example, since Mr. Lewis' demands for a health service to his miners has been granted and since many other unions are making or have been granted similar demands, have not shown the enthusiasm which previously was exhibited. Likewise former military men seem to feel that these bills will subject them to heavy taxation in spite of the fact that the Veterans Administration is apparently prepared to give medical care to all of the soldiers and other members of the armed forces who participated in World War I and in Global War II.

The published reports that are appearing in the Journal of the American Medical Association of the hearings of the Senate Committee on Education and Labor would seem to show that there is considerable amount of sentiment against the bills not only by the medical profession but by other groups. To the medical man the bills seem so ridiculous and the arguments so many against them that it does not seem possible that they could pass an intelligent Congress. However, we never know what may emanate from the Congress and our efforts to defeat the bills should not be relaxed.

One of the interesting features of these bills which rates so high in the thoughts of the medical man is the general lack of interest in them throughout the country. Apparently most people do not even know about the bills as shown by a recent Gallup Poll. These medical insurance bills, according to the poll, were known to only four in every ten persons questioned and the majority of the forty per cent who knew that there were such bills were unfamiliar with their provisions and had given very little thought to how they would affect the general economy of the country. Furthermore of those questioned the majority felt that they would not be willing to pay any more for medical insurance than they are now paying for doctor and hospital bills and about half of those quizzed said they would be unwilling to pay as much.

Lastly, the opinion was expressed by less than half of the people who were questioned, that they would get as good medical service under government supervision as they are now getting. Certainly this poll would indicate that the citizenry of the United States are not particularly inter-

ested in the bills nor do the majority of those who know anything about the bills feel that they would get any better medical service than they are now obtaining.

THE ANTI-VIVISECTIONISTS

It is earnestly to be hoped that many doctors may have the opportunity of reading Mr. Bernard DeVoto who writes the section entitled "The Easy Chair" in each month's number of the Harper's Magazine. In the June edition of this long existing and well known publication, he lights into the anti-vivisectionists in a way that the medical profession would hardly have the temerity to do. Mr. DeVoto's expressions and his writings are so superior that we may be pardoned for quoting them rather extensively.

In the first place Mr. DeVoto points out that the so-called anti-vivisection campaigns are carried on by a group of professionals who are in the campaigns not for unselfish purposes, but for what they can get out of them financially. They enlist unpaid volunteers, for the most part "elderly sentimentalists . . . escapees, the perpetually indignant, the perpetually confused . . . They are earnest bewildered souls . . . probably with deflected affections and certainly with all-embracing ignorance and a vigorous resistance to thought." These are the type of people who represent the volunteer workers. What Mr. DeVoto can not understand is why the "front men and women" will sign the literature and manifestos which are prepared by the professionals. "Their zeal is a danger to all of us, but their irresponsibility is a greater danger . . . it is not fair to dismiss them as necessarily either fools or liars—though it is difficult to believe that they are always unaware that the statements they issue and the literature they sign are mendacious, composed almost entirely of misrepresentations, distortions, and misstatements". The essayist goes even further and states that their appearance of benevolence and kindness "covers a pathological misanthropy, a residue of primitive totemism, and a still more primitive destructiveness". He contends that the pathologic champion of animals is a pathologic hater of men.

Mr. DeVoto states that to answer these people is both foolish and impossible. Probably every honorary officer of an anti-vivisection society owes his life or that of a member of his family to medical and surgical experiments on dogs. He points out that what we know of physiology has been learned almost entirely from animal experimentation; almost all advances in surgical technic have come from experiments on animals; what we know about immunity and about the use of vaccines and antitoxins and serums has been learned from the same source. When a sulpha drug is given, or penicillin, or even a barbiturate, when a woman and her infant survive a difficult delivery the sedative and anesthesia and the surgical technic are the result of animal investigation. He writes that "one of the few undebatable triumphants of civilization, progress in medical science, rests on animal experimentation."

In his concluding paragraph he notes that at times there appear small religious sects in the desperately uneducated which in their superstitious ignorance often show a compulsive frenzy which seems diseased. "The charity that excuses ignorance can not be extended to them (the anti-vivisectionists), for mostly they are well educated and economically fortunate above the average. They must be thought of as at best neurotic and at worst corrupt."

DIAGNOSIS OF CANCER

One of the most fascinating chapters in the book of diagnosis has to do with the recognition of cancer as developed by the technic of Dr. George N. Papanicolaou.* To recall his original observations which appeared some years ago, he showed that diagnosis of cancer of the female genitalia might be made early in the course of the disease through the study of vaginal smears. Very little interest was aroused in

*Papanicolaou, George N.: Diagnostic value of exfoliated cells from cancerous tissue, J. A. M. A., 131:372, 1946.

his observation until within the last few years. Now, however, it has become part of the routine of the periodic health examination to have vaginal smears made, knowing that malignancy of the genital tract may be recognized through the appearance of pathologic cells in the smear more readily, more promptly and earlier than by any other method. Furthermore any woman who has symptoms suggestive of carcinoma of the uterus should have a vaginal smear made by her physician and studied by a competent pathologist.

The fact that the malignant cells exfoliate from the uterus is now well recognized but as a recent paper of this well known investigator shows, it is not generally accepted that malignancy may be recognized elsewhere in the body early in the course of the disease through the findings of pathologic cells in the excretions or secretions. A careful study of the sputum may show abnormal cells which may lead to the diagnosis of bronchiogenic carcinoma before the cancer can be visualized by the endoscope. The gastric contents may show cancer cells very early in the course of the development of the malignancy. The urinary sedimentation will do the same. In fact the diagnosis of early carcinoma may be made by the study of the smears from the secretions and excretions with proper technic, in a large number of cases. It is to be hoped that the studies of Dr. Papanicolaou will be carried out extensively in laboratories throughout the country. Certainly the results that the author has had are remarkable but as he says they are still far from being complete and it will be many years before the potentialities of this new diagnostic approach have been thoroughly explored by many investigators.

ORGANIZATION SECTION

The Executive Committee dedicates this section to the members of the Louisiana State Medical Society, feeling that a proper discussion of salient issues will contribute to the understanding and fortification of our Society.

An informed profession should be a wise one.

EMIC PROGRAM

With further reference to termination of the EMIC Program by the State Society the Executive Committee at a meeting on June 8 ruled that ANY CASE PREGNANT BEFORE THE TERMINATION OF THE EMIC PLAN (MAY 8, 1946) MAY BE ACCEPTED BY MEMBERS OF THE SOCIETY.

SENATE BILL 2143

Special attention is called to Senate Bill 2143, recently introduced by Senator Taft for himself, Senator Ball and Senator Smith, known as the "National Health Bill". This bill developed as a result of differences of opinion on the Wagner-Murray Bill S.1606, and might be offered as a substitute to the Committee on Education and Labor to which has been assigned S.1606. The secretary has had occasion to review this bill and finds the basic principles to be very sound. There are a few necessary amendments which should be made to meet the full requirements of the medical profession in their relation to the public on any prepayment plan. A very fine review of this bill recently occurred in the Journal of the American Medical Association (May 25, 1946, Page 338). .

COUNCIL ON MEDICAL SERVICE AND PUBLIC RELATIONS

At the meeting of the Executive Committee on June 8 plans for a Council on Medical Service and Public Relations in the State Society which had been approved by the House of Delegates were discussed. It was decided that the president should appoint a committee to work with him in planning details for such a council; these to be submitted to the Executive Committee

for final action. It was also agreed that Dr. Peacock, as delegate to the A.M.A., should be requested to represent our Society at a meeting of state chairmen of councils on medical service and public relations to be held in San Francisco during the time of the A.M.A. meeting and that he be instructed to submit a report to the special committee on his return.

PREPAYMENT MEDICAL SERVICE

Dr. O. B. Owens, Chairman of the Committee on Prepayment Medical Service presented to the Executive Committee a schematic diagram of the proposed set-up of the Louisiana Physicians Service, Inc., and asked for approval of the following, which was granted: 1. Material as presented in rough draft as a guiding principle for further work by the committee and the attorney. 2. Authorization for the Board of Directors to employ Mr. Barret (of Shreveport) or some other well-qualified insurance attorney, to draw the necessary legal documents and serve as attorney for the Board in the organization and early period of operation of the plan; the fee for which would be paid as an organization expense by the Corporation. 3. Authorization for the proper officers of the Louisiana State Medical Society to make available for deposit with the State of Louisiana Insurance Department the necessary initial deposit, together with the sum of $10,000 for implementation of the organization and operation of the plan; this amount to be made available upon submission by the attorney of the necessary loan agreement, as indicated in the documentary outline. 4. Authorization for the Board of Directors to enter into contract negotiations with local hospitalization units throughout the state or other organizations or individuals for administration of the plan in specified areas of the state. 5. Authorization of the use of press, radio, pamphlet or other forms of advertising by the Board and its members, including a statement that the plan is sponsored and approved by the Louisiana State Medical Society and its constituent bodies and members. 6. Authorization for the Board to prepare copy of printed matter and the taking of bids and awarding of contracts for printing of the necessary policies, contract forms, stationery and advertising material. 7 Authorization for the Board to employ either on a temporary or permanent basis, as later need may indicate, a trained surgical plan executive. 8. Authorization for the Board, through its contractive representatives, at the proper time as defined by the Insurance Department, to begin soliciting and enrolling subscriber groups.

It has been further decided that the headquarters for the Louisiana Physicians Service, Inc. will be in the domicile of the State Medical Society in New Orleans.

Dr. Owens and his committee are to be congratulated on the excellent service they have rendered to our organization in consideration of plans for voluntary prepayment medical service in the state.

LOUISIANA LEGISLATION

The Committee on Public Policy and Legislation has been extremely active during recent weeks in connection with proposed legislation which will affect the medical profession of this state. Outstanding in their accomplishments is success in having the Senate chiropractic bill defeated and a similar bill in the House withdrawn. Also House Bill 38, in re temporary license to foreigners to practice medicine in Louisiana, which the House of Delegates at the annual meeting went on record as opposing, was after much effort on the part of our legislative committee, defeated.

The members of this important committee are still giving much time and thought to other legislative matters to be considered in the future and much gratitude should be expressed to them for their willingness to assist organized medicine in this manner.

RESOLUTION IN RE CHIROPRACTORS

The following resolution has been sent to each component society in the state and is published here so that members may report to their local organizations such illegal practice of which they have knowledge in

their parish: Be it resolved by the Executive Committee of the Louisiana State Medical Society in session in New Orleans on June 8, 1946, that the parish and district medical societies of the State of Louisiana be authorized to request of the Louisiana State Board of Medical Examiners that they start legal proceedings against any and all chiropractors now applying their supposed profession in opposition to our present medical laws. Senate Bill No. 66 of the 1936 Legislature which would legalize chiropractors in this state was voted down by the Committee on Education and Quarantine on June 5. There was only one dissenting vote. Most of the co-authors of the bill when they found out that the medical profession was against this bill were in favor of withdrawing the bill. We are now assured that the state legislature and representatives of the people of the state do not want chiropractors attempting to practice medicine here. Be it further resolved that a copy of this resolution be sent to every parish and district medical society in the state advising them to request the State Board of Medical Examiners to start legal proceedings against all illegal practitioners as soon as possible. Be it further resolved that the State Medical Society also request the State Board of Medical Examiners to assist in prosecuting these men wherever necessary.

1947 ANNUAL MEETING

The dates of May 12-14, 1947 have been selected for the meeting of the State Society to be held in New Orleans next year and the president, Dr. Rhett McMahon, has appointed the following members to serve as chairmen of scientific sections for the meeting: Dr. John L. Beven, Baton Rouge, Bacteriology and Pathology; Dr. R. Phillips, Baton Rouge, Ear, Nose and Throat; Dr. Lionel F. Lorio, Baton Rouge, Eye; Dr. James E. Toups, Baton Rouge, Gastro-enterology; Dr. Henry C. Hatcher, Baton Rouge, General Surgery; Dr. W. D. Beacham, New Orleans, Gynecology; Dr. Phillip H. Jones, New Orleans, Medicine and Therapeutics; Dr. Arthur D. Long, Jr., Baton Rouge, Nervous Diseases; Dr. Paul W. Winder, Shreveport, Obstetrics; Dr. T. Jeff McHugh, Baton Rouge, Orthopedic Surgery; Dr. David S. Miller Baton Rouge, Pediatrics; Dr. Bernard E. Nelken, Baton Rouge, Public Health and Sanitation; Dr. Lester J. Williams, Baton Rouge, Radiology; Dr. John G. Menville, New Orleans, Urology.

TRANSACTIONS OF ORLEANS PARISH MEDICAL SOCIETY

July 8. Scientific Meeting, 8 p. m.

July 17. Clinico-pathologic Conference, Marine Hospital, 7:30 p. m.

July 18. Clinico-pathologic Conference, Touro Infirmary, 12 noon.

July 24. Catholic Physicians' Guild, 8 p. m.

July 25. De Paul Sanitarium Staff, 8 p. m.

July 26. L. S. U. Faculty Club, 8 p. m.
New Orleans Hospital Dispensary for Women and Children Staff, 8 p. m.
Ochsner Clinic Staff, 8:30 p. m.

July 31. Clinico-pathologic Conference, Marine Hospital, 7:30 p. m.

Aug. 1. Clinico-pathologic Conference, Touro Infirmary, 12 noon.
Executive Committee, Baptist Hospital, 8 p. m.

Aug. 5. Board of Directors, Orleans Parish Medical Society, 8 p. m.

Every Tuesday, Medical Toastmasters, New Orleans Athletic Club, 6:30 p. m.

Every Wednesday, Medical Discussions, Radio Station WDSU, 9:15 p. m.

Dr. Samuel Barkoff gave a paper on "The Psychoanalytic Treatment of Bronchial Asthma" at the Washington-Baltimore Psychoanalytic Society meeting in Baltimore on May 12.

Dr. Ernest C. Faust addressed the 27th meeting of the American College of Physicians in Philadelphia, May 17.

Dr. Hiram W. Kostmayer was recently elected to honorary membership in the Tulane History of Medicine Society.

Dr. Lucien A. LeDoux recently attended the forty-seventh annual meeting of the American

Therapeutic Society in Atlantic City, May 11-12. Dr. LeDoux is second vice-president of the society.

Dr. Alton Ochsner recently addressed Loyola university students on the topic "Effects of Tobacco on the Human Body." The lecture was sponsored by Beta Epsilon Upsilon, national honorary medical technology society at Loyola.

Dr. Thomas Benton Sellers attended the mid-year clinics of the American Association of Obstetricians, Gynecologists and Abdominal Surgeons held in Chicago recently.

Dr. H. Ashton Thomas was appointed a member of the Board of the City Health Department; Drs. Boni J. DeLaureal and John M. Whitney were re-appointed.

Dr. Julius Lane Wilson was re-elected president of the Louisiana Tuberculosis Association at the annual meeting of that organization in Alexandria, May 5. Other members of this Society elected to office were: Drs. Sydney Jacobs and Maurice Campagna, vice-presidents; Drs. J. A. Danna, Edgar Hull, John H. Musser, I. L. Robbins, Suzanne Schaefer and John M. Whitney, members of the executive committee.

Congratulations to Dr. and Mrs. Arthur Calix on the arrival of Kathleen Elizabeth May 6.

MEDICAL TOASTMASTER

Dr. Edwin L. Zander was recently elected president of the Medical Toastmasters. Other officers elected were: Dr. Philip H. Jones, vice-president; Dr. Lawrence J. O'Neil, secretary-treasurer; Dr. J. A. Colclough, sergeant-at-arms; and Dr. Charles A. Bahn, deputy.

WELCOME HOME

Dr. Norton M. Voorhies was recently separated from military service. He has resumed practice at 1712 Pere Marquette Bldg.

LOUISIANA STATE MEDICAL SOCIETY NEWS

CALENDAR

PARISH AND DISTRICT MEDICAL SOCIETY MEETINGS

Society	Date	Place
East Baton Rouge	Second Wednesday of every month	Baton Rouge
Morehouse	Second Tuesday of every month	Bastrop
Orleans	Second Monday of every month	New Orleans
Ouachita	First Thursday of very month	Monroe
Rapides	First Monday of every month	Alexandria
Sabine	First Wednesday of every month	
Second District	Third Thursday of every month	
Shreveport	First Tuesday of every month	Shreveport
Vernon	First Thursday of every month	

NEW DEAN OF L. S. U.

The board of supervisors of Louisiana State University announce the appointment of Dr. Vernon William Lippard of Columbia University as dean of the university medical school. Dr. Lippard is a graduate of Yale Medical School and for several years was a member of the Cornell University faculty. He was in the army with the rank of lieutenant colonel and since his release from military service has been associate dean of the medical school at Columbia University. He is one of the well known younger pediatricians in this country being certified by the American Board of Pediatrics and a member of the Society for Pediatric Research as well as county, state and national medical organizations. He is a member of Alpha Omega and Sigma Xi honorary societies.

Dr. Lippard will succeed Dr. George W. McCoy who has been acting dean since the resignation of Dr. Wilbur C. Smith.

LAKESHORE HOSPITAL

The new Lakeshore Hospital was opened for patients on Saturday, June 1. On Sunday, June 2, a reception was given to the medical profession and others at which time the hospital could be inspected and the arrangements that had been made to take care of the patients were shown to the visitors. The hospital is conducted by the New Orleans Medical Foundation, most of whom are physicians who have served in the armed forces. Dr. Charles B. Odom is president of the Foundation and to him as well as to others of the officers a great deal of credit should be given for obtaining these additional hospital beds so badly needed in New Orleans. The Lakeshore Hospital is open to all members of the medical profession belonging to the Orleans Parish Medical Society and promises to help relieve the exigency for beds in the city. Mr. Evert E. Moody is director of the new institution.

NEW CHARITY HOSPITAL APPOINTMENTS

Dr. Roscoe L. Pullen, who for the past several years has been assistant director of the New Orleans Charity Hospital, resigned effective July 1. To replace Dr. Pullen, Dr. O. P. Daly, director of the institution, has appointed Dr. Jacques Magne, who will be at the head of the medical division of the hospital and Dr. Joseph Dills, who will have charge of the surgical division.

Dr. Magne served with distinction throughout the war, obtaining the rank of lieutenant colonel. He is a New Orleanian who graduated from Tulane in 1938 and became a resident on the medical service until called to active duty in 1941.

Dr. Dills is a graduate of the Washington University in St. Louis and since his graduation in 1941 he has been connected with the Charity Hospital, first as an intern then as admitting physician and finally as surgical resident. He was appointed on the L. S. U. surgical staff on July 1, 1943.

THE NEW ORLEANS GRADUATE MEDICAL ASSEMBLY

The New Orleans Graduate Medical Assembly has elected the following members for office for the year 1946-1947: Dr. Joseph S. D'Antoni, President-elect; Dr. Randolph Lyons, First Vice-president; Dr. H. Ashton Thomas, Second Vice-president; Dr. C. S. Holbrook, Third Vice-president; Dr. Max M. Green, Secretary; Dr. Edwin H. Lawson, Treasurer; Dr. Barrett Kennedy, Director of Program; Dr. J. O. Weilbaecher, Jr., Asst. Director of Program; Dr. Ambrose H. Storck, Asst. Director of Program. Executive Committee: Dr. Howard R. Mahorner (two year term), Dr. Lucien A. Fortier (two year term).

The following officers elected in 1944 who will also serve for the coming year are as follows: Dr. William H. Gillentine, President. Executive Committee: Dr. L. C. Chamberlain, Retiring President; Dr. Frederick F. Boyce, Dr. Charles B. Odom.

DE PAUL SANITARIUM

The regular monthly meeting of the Medical Staff of De Paul Sanitarium was called to order at 8:00 p.m. on May 23, 1946, with Drs. Friedrichs, May, Otis, Beach, Barkoff, Dupuy, Hunter Harris, Holbrook, Anderson, H. Colomb, Hite, Connely, Monroe and Dubos in attendance.

The scientific program began with a discussion by Dr. Holbrook of Case No. 4646, that of a white female approximately five feet two inches in height, weighing 287 pounds, first seen in 1923 and again in 1930. At that time she was suffering from depression and melancholia. One month ago she was again seen for the same symptoms and admitted to De Paul, but because of her extreme obesity and hypertension she was considered a poor risk for electroshock and therapy was limited to simple palliative measures. She was placed on a low caloric diet and given thyroid medication. With good nursing care she showed sufficient improvement to leave the institution and return home within one month's time. The case was further discussed by Drs. Barkoff, Otis and Dubos.

Dr. Beach next summarized briefly the properties, dangers and uses of curare in relationship to shock therapy. This topic was further discussed by Drs. Holbrook and Anderson.

At the request of the president of the staff the minutes of the previous meeting were read and after due motioning and seconding were adopted as read.

Dr. Otis as Chairman of the Records Committee read the reports of the various departments following which Dr. Friedrichs, Chairman of the Library Committee reported additional donations to the Lewis A. Golden Collection Fund.

There being no further business the meeting adjourned at 9:10 p.m., followed by the serving of refreshments.

Louis J. Dubos, M. D., Secreary.

LOUISIANA PHYSICIANS PARTICIPATING IN THE SCIENTIFIC PROGRAM OF THE A. M. A. MEETING

The following doctors from Louisiana have presented papers or exhibits at the annual meeting of the A. M. A. which started Monday, July 1, in San Francisco.

In the general scientific meeting Dr. Alton Ochsner, professor of Surgery at Tulane Medical School, gave a lecture on thrombosis and embolism and participated in the discussion on the problem of phlebothrombosis and thrombophlebitis. Colonel M. E. DeBakey of New Orleans, was one of the joint authors on the use of streptomycin in clinical practice. Dr. Champ Lyons, Professor of Clinical Surgery at Tulane Medical School, read a paper on chemotherapy in wound management. Dr. Ralph V. Platou, Professor of Pediatrics at Tulane Medical School, addressed the section on dermatology and syphilology on penicillin therapy in early congenital syphilis. Two New Orleans doctors appeared before the section on gastroenterology and proctology, Dr. Donovan C. Browne, Assistant Professor of Medicine at Tulane, discussed the treatment of intestinal conditions as based on disordered functions, and Dr. D. N. Silverman, Professor of Clinical Medicine at L. S. U. Medical School and Dr. Alan N. Leslie had a paper on intestinal tumors of dysentery origin.

The Chairman's address before the section on anesthesiology was given by Dr. Ansel M. Caine, Assistant Professor of Surgery at Tulane Medical School. In this same section Dr. John Adriani, Clinical Assistant Professor in anesthesia at L. S. U. Medical School, was one of a group of

authors who spoke on subarachnoid use of vasoconstrictors in spinal anesthesia.

At the section exhibits, Dr. George E. Burch, Associate Professor of Medicine at Tulane Medical School and Dr. Travis Winsor, formerly on the staff of Tulane Medical School, and Dr. James L. Kimball had an exhibit on the clinical applications of venous pressure measurements. Dr. John Adriani and Dr. Ray T. Parmley had an exhibit from Charity Hospital and Louisiana State University School of Medicine on saddle block anesthesia. Dr. Guy A. Caldwell, Professor of Orthopedic Surgery at Tulane Medical School, and Dr. Donald Imrie of the Ochsner Clinic, had a motion picture on the analysis of muscle function in poliomyelitis. Colonel Roy H. Turner, Associate Professor of Medicine at Tulane Medical School, participated in the Medical Consultants Division of the U. S. Army, his exhibit showing diagnosis, course and treatment of infectious hepatitis.

NEWS ITEMS

Dr. Ernest Càrroll Faust has received a Medal of Freedom for the work which he has done on schistosomiasis. It may be recalled that Dr. Faust was invited by the government to make a study of the problem of schistosomiasis in the Phillipines and western theatre and spent some months in this area.

Dr. Alton Ochsner has been selected as the president-elect of the American Association for Thoracic Surgery.

Dr. Wilbur C. Smith has been appointed director of student health and physical activities at the University of Wyoming.

PHYSICIAN WANTED

A physician is needed in Franklin, Louisiana to take over practice of a physician recently deceased. Office space and equipment and also records of the former doctor are available. For further information contact the office of the State Medical Society.

MISSISSIPPI VALLEY MEDICAL SOCIETY

The eleventh annual meeting of the Mississippi Valley Medical Society will be held at the Hotel Jefferson, St. Louis, September 25-27.

THE AMERICAN CONGRESS OF PHYSICAL MEDICINE

Will hold its twenty-fourth annual scientific and clinical session September 4, 5, 6 and 7, inclusive, at the Hotel Pennsylvania in New York. Scientific and clinical sessions will be given each day. All sessions will be open to members of the medical profession in good standing with the American Medical Association. In addition to the scientific sessions, the annual instruction courses will be held September 4, 5, and 6. These courses will be open to physicians and to therapists registered with the American Registry of Physical Therapy Technicians. For information concerning the convention and the instruction course, address the American Congress of Physical Medicine, 30 North Michigan Avenue, Chicago 2, Illinois.

INTERNATIONALLY KNOWN SPEAKERS AT COLLEGE OF SURGEONS ASSEMBLY IN DETROIT

Mr. Hamilton Bailey of London, England, will visit Detroit in October to deliver an address at the Eleventh Assembly of the United States Chapter, International College of Surgeons. His subject will be "Impending Death under Anesthesia".

Other eminent speakers and clinicians who will appear at the I. C. of S. clinics, and the Assembly to be held in Detroit's Masonic Temple, October 21, 22 and 23, include: Dr. Albert Jirasek of Prague, Dr. Francisco Grana of Lima, Peru, Dr. Lyon Appleby, Vancouver, B. C., Dr. Felipe Carranza of Buenos Aires, Dr. W. Wayne Babcock of Philadelphia, Dr. R. W. McNealy, Chicago, Dr. Wm. C. MacCarty, Rochester, Minn., Dr. Edwin L. Zander, New Orleans, Dr. Rudolph Nisson, New York, Dr. Max Thorek, Chicago, Dr. H. E. Billig, Los Angeles, Dr. S. W. Harrington, Rochester, Minn., and others.

Copy of program and detailed information, including housing arrangements, may be obtained by writing Dr. L. J. Gariepy, Secretary, 16401 Grand River Avenue, Detroit 27, Michigan.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY, INC.

The annual meeting of the Board was held in Chicago, Illinois, from May 5 to May 11, 1946, at which time one hundred forty-one candidates were certified.

A number of changes in Board regulations and requirements were put into effect. Among these is the requirement that case records must now be forwarded to the Secretary's Office from thirty to sixty days after the candidate has received notice of his eligibility for admission to the examinations for certification. At this meeting the Board also ruled that it will not accept the nine months' residency as an academic year toward years of training requirements following the termination of the official period of intern and residency acceleration, April 1, 1946.

The next written examination (Part I) for all candidates wil be held in various cities of the United States and Canada on Friday, February 7, 1947 at 2:00 p. m. Candidates in military service are requested to keep the Secretary's Office closely informed of changes in address.

Applications are now being received for the 1947 examinations. Closing dates for these applications will be November 1, 1946.

For further information and application blanks address Paul Titus, M. D., Secretary, 1015 Highland Building, Pittsburgh, 6, Pennsylvania.

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ARMY LOWERS DISCHARGE REQUIREMENTS FOR MEDICAL CORPS OFFICERS

Discharge requirements for Medical Corps general duty officers were reduced on May 1 from 39 to 30 months service and from 45 to 39 months for certain specialist officers.

Requirement on points remains at 60 and the age limit at 45 years.

This move will result in the discharge of approximately 2,000 doctors and will leave about 3,000 Medical Corps officers not included in the ranks of the Regular Army, volunteers and Army Specialized Training Program graduates.

Officers returning from overseas will be discharged automatically if they would become eligible for discharge within the following six months instead of four months as previously stipulated. Also, Army doctors overseas regardless of their military occupational specialty classification, will be separated or enroute to the United States within 60 days of date of eligibility.

That the Army is demobilizing its Medical Corps officers as quickly as possible without jeopardizing the treatment of patients is shown in the announcement that since VE Day about 32,000 have been discharged.

The specialists who require the longer term of service for discharge are gastroenterologists, cardiologists, urologists, dermatologists, anaesthetists, general surgeons, physical therapists, radiologists, pathologists, orthopedic surgeons, internal medicine specialists and eye, ear and nose specialists.

INFECTIOUS DISEASES IN LOUISIANA

The weekly morbidity report for the State of Louisiana for the week ending April 27 showed measles leading all other reportable diseases with 285 cases. Following in numbers greater than ten were hookworm infestation 57, pulmonary tuberculosis 50, influenza 47, malaria 35, mumps 33 and septic sore throat 26. There was one case of poliomyelitis reported this week in Webster Parish. There is something peculiar about the reporting of some of these diseases. In the previous week there were only two cases of cancer listed and six of unclassified pneumonia whereas for the week ending May 4 there are 193 cases of unclassified pneumonia and 166 incidences of cancer. Other prevalent diseases include 119 cases of measles, 60 of pneumococcic pneumonia, 40 of whooping cough, 38 of mumps, 28 of pulmonary tuberculosis, 21 of hookworm infestation, 15 of scarlet fever, 13 of amebiasis and 12 of malaria. Of the rarer diseases, poliomyelitis was reported in one instance in Orleans Parish. For the week which came to a close on May 11 the six diseases which occurred in numbers greater than ten were measles 190 cases, pulmonary tuberculosis 48, whooping cough 25, mumps 23, unclassified pneumonia 19 and German measles 17. This week there was another case of poliomyelitis, this time listed from Lafayette Parish. For the week which ended May 18 the report shows obviously that measles was still quite prevalent, there being 165 cases listed, followed by 40 of pulmonary tuberculosis, 36 of mumps, 29 of malaria, 20 of unclassified pneumonia and 12 each of whooping cough and septic sore throat. There were five cases of poliomyelitis listed this week, no two of which originated in any one parish. For the week which closed May 25 there were only 64 cases of measles listed, 27 of pulmonary tuberculosis and 18 of mumps. No other disease occurred in number greater than ten. Again, there were five cases of poliomyelitis reported in the state.

The Bureau of Epidemiology of the Louisiana State Board of Health now reports venereal disease incidence as a separate report. For the month of March there were listed 2,091 cases of gonorrhea, 1,793 of syphilis, 64 of chancroid, 32 of granuloma inguinale and eight of lympopathia venereum. For the month of April there were listed 1,795 cases of syphilis, 1,656 of gonorrhea, 48 of chancroid, 30 of granuloma inguinale and eight of lymphopathia venereum.

HEALTH IN NEW ORLEANS

The Bureau of the Census, Department of Commerce reported that for the week ending May 11 there occurred in the City of New Orleans 133 deaths divided 85 white and 48 colored. Of this 133, 11 were children under one year of age. The following week showed a very marked decrease; the total deaths being only 102 as contrasted with the previous three year average of 133. Of these deaths 67 were in the white population, 35 in the colored and seven were in infants. There was a slight increase in the number of deaths for the week ending May 25 but this was still below the three year average. The deaths were apportioned 67 white, 52 colored and the total number of deaths in children was only seven. For the week which closed June 1 the remarkably low death rate was still maintained. There were only 117 deaths in the city, 69 of which were in the white population and 48 in the colored but the infant deaths had risen to 18. The death rate for the week ending June 18 was higher than for the previous week but still below the three year average. In this particular week the 131 deaths in the city were divided 74 white, 57 colored and 11 infants.

CORRECTION

In the article by Robert A. Katz, M. D., "Impending Ischemic Gangrene" in the June issue, page 551, paragraph one, beginning with line 13, reads as follows:

Within three days, despite the fact that the lower extremity is kept in a dependent position for a period up to three hours, the ulcer on the lower half of the leg has decreased about one-half in size and the portion which has not been covered by epithelium is covered with healthy granulation tissue.

This should read: Within three days the pain was entirely relieved and has not returned despite the fact that the lower extremity is kept in a dependent position for periods up to three hours. The ulcer on the lower half of the leg has decreased about one-half in size and the portion which has not been covered by epithelium is covered with healthy granulation tissue.

WOMAN'S AUXILIARY

LUNCHEON FOR WIVES OF RETURNING DOCTORS

In honoring the doctors who have recently returned from service in the armed forces, Mrs. M. C. Wiginton, press and publicity chairman of the Woman's Auxiliary, State Medical Society, gave a delightful luncheon at her home. Wives of the doctors were special guests and a number of out-of-town ladies were in attendance, including Mrs. Arthur Long of Baton Rouge, state president of the auxiliary, and Mrs. F. U. Darby, also of Baton Rouge, president-elect of the East Baton Rouge Auxiliary. Mrs. Roy Carl Young of Covington, who is a past president of the Woman's Auxiliary of the State Medical Society, was also present. She is now serving as councilor for the sixth district. Mrs. Young was accompanied by Mrs. H. E. Cannon of Covington.

Those attending from Tangipahoa Parish were as follows: Mrs. Glenn T. Scott and Mrs. Collins P. Lipscomb of Ponchatoula; Mrs. DeLoach Thames, Mrs. C. D. Alessi, Mrs. S. J. Cali, Mrs. A. J. Feder, of Hammond; Mrs. Jesse H. McClendon of Amite.

Following the luncheon Mrs. Long and Mrs. Young gave interesting talks on the work being done by the auxiliaries and the importance of organizing, especially now when everyone is vitally interested in the proposed Murray-Wagner-Dingell bills and others of similar note, which means enforced socialized medicine on the general public. It was pointed out that through close contact with the medical profession the auxiliaries realize the danger of such bills being imposed upon the people, hence feel willing to do everything possible to assist in securing the proper information regarding the danger of such legislation.

Wives of doctors of the parish agreed to reorganize and the following officers were elected: President, Mrs. Glenn T. Scott of Ponchatoula; President-elect, Mrs. DeLoach Thames of Hammond; Vice-president and Program Chairman, Mrs. S. J. Cali of Hammond; Secretary, Mrs. Collins Lipcomb of Ponchatoula; Treasurer, Mrs. C. D. Alessi of Hammond.

Various chairmen are to be appointed by the president later, it was explained. It was stressed that the objects of the auxiliary are to interpret the aims of the medical profession to other organizations interested in the promotion of health education, to assist in the entertainment of the medical society, to encourage friendliness among families of the medical profession, and to do work approved by the advisory council of the American Medical Association. It was pointed out that the wives of doctors working together as an auxiliary could serve their respective communities efficiently and make community life much better. The ladies present all expressed a desire that they be called upon whenever help is needed in any of the communities of Tangipahoa Parish.

Reports from over the state concerning the activities of the auxiliaries should be made to Mrs. Wiginton at Hammond, in her capacity as press and publicity chairman of the Woman's Auxiliary to the Louisiana State Medical Society.

TEA FOR MRS. ARTHUR LONG

Honoring Mrs. Arthur Long recently at the Woman's Clubhouse in Baton Rouge were members of her own auxiliary and guests from out of town including groups from New Orleans and surrounding communities. Guests arrived at the clubhouse between the hours of three and five o'clock, being greeted at the doorway by Mrs. Rhett McMahon, whose husband is the newly-installed president of the State Medical Society and Mrs. B. E. Nelken. Guests were registered by Mrs. Eugene Toups. The tea tables were presided over by Mrs. Lionel Lorio, Mrs. J. Webb McGehee, Mrs. Lester J. Williams and Mrs. Henry Voss.

Heading the receiving line was Mrs. Charles E. Allen, Jr., the new president of the Baton Rouge Auxiliary, followed by Mrs. Long, Mrs. Frank Jones, state corresponding secretary, Mrs. Russell Kuehnle, state treasurer, Mrs. John L. Beven and Mrs. Felix Boizelle, general chairmen of the tea, Mrs. F. U. Darby, president-elect of the Baton Rouge Auxiliary, and Mrs. Cecil Lorio. Mrs. Wiley A. Dial was in charge of the tea tables. Miss Celeste Jamerson played a soft accompaniment at the piano throughout the afternoon.

The group of tea girls who served during the afternoon included Mrs. Guy Riche, Jr., Mrs. George Thomas, Mrs. Sterling Albritton, Mrs. McHugh Simmons, Mrs. William Cook, Mrs. Courtland P. Smith and Mrs. Claude McConnell.

Out of town guests at the tea included Mrs. Carroll F. Gelbke, president of the New Orleans Auxiliary, Mrs. James W. Warren, president-elect of the State Auxiliary, Mrs. Paul G. Lacroix, past president of the State Auxiliary and Mrs. J. S. Dunn, Mrs. C. Grenes Cole, Mrs. J. Kelly Stone, Mrs. C. L. Peacock and Mrs. Roy B. Harrison, all of New Orleans; Mrs. Rhodes Spedale, Plaquemine, past state president; Mrs. Charles J. Wise, Angola; Mrs. William Roberts, Clinton; Mrs. Emerson W. Singletary, Baker; Mrs. D. B. Barber and Miss Jane Hall, of Alexandria.

BOOK REVIEWS

Principles of Dynamic Psychiatry, Including an Integrative Approach to Abnormal and Clinical Psychology: By Jules H. Masserman, M. D. Philadelphia, W. B. Saunders Co. 1946. Pp. 322. Price $4.00.

Just a glance through this volume discloses some of its brilliance, and deeper study of it reveals its profound knowledge. The author wrote it to get into print certain fundamentals of modern dynamic psychiatry, heretofore being taught only through lectures and percepts, so he could divert his efforts to clinical teaching and guidance to which reading alone must forever remain supplementary.

In Part I, Chapter 6, it is related that while affective, regressive and schizophrenic defense mechanisms are therein grouped together not because of their close relationships or similarity, but for the reason that when pervasive and excessive they give rise to definite types of behavioral aberrations and such reactions also have their roots in various "normal" modes of adaptive behavior.

On page 66—Cases: Acute regression, combat neurosis—appears an excellent example of an illustrative material note: "A soldier, however well-disciplined and self-reliant, if subjected overlong to physical exhaustion and the intolerable hell of combat and carnage in the ever-present shadow of death, will eventually reach his limit of tolerance and will thereafter show a gradual dissolution of adult habit-patterns and an accelerating return to childlike and then infantile behavior. First his intellectual interests and activities will become dulled and his affective reactions progressively more irritable and primitive; concurrently, he will begin to neglect habits of personal hygiene, even to the point of careless evacuation and soiling. Next, his fantasies may become preoccupied with hazy dreaming of the comforts and securities of his own home; finally, in sudden desperate denial of all mature considerations of prestige, duty, discipline or even physical danger, he may abandon his weapon, cry out against all about him and fall to the earth sobbing piteously and inconsolably for his mother. Obviously, during this extreme reaction, threats of further discipline or even death are useless; the soldier must be evacuated as a psychiatric casualty, permitted for the time being to cling emotionally to some kindly therapist as a parent surrogate, and thereafter treated by every means at hand to restore his self-confidence, his group loyalties and his normal defenses against anxiety, before his regression becomes fixed at the level of phobia-ridden, helpless passivity."

The purposes of this work are, then, to provide an orientative introduction to the principles of modern dynamic psychiatry, to outline their application to the technics of clinical diagnosis, and to demonstrate the rationale and methods of effective therapy. This book is a most notable, important contribution to medical science and, if there is a better one, the reviewer has not seen it.

C. P. MAY, M. D.

Voies et Centres Nerveux: By J. Delmas and A. Delmas (both of the Faculty of Medicine at Montpellier). Paris, Masson et Cie., 1946. Pp. 164, figs. 92. 270 fr.

This little paper-bound volume, published in the series "Libraires de L'Académie de Médecine," is offered as an anatomic-physiologic introduction to neurology. In keeping with the objectives of such an introduction, the subject matter is condensed and simplified. The organization is well planned for the purpose of correlating anatomy and functional relationships. The illustrations, all in the form of simple line drawings, are judiciously selected and instructive. The book contains a few footnote references to original literature. They represent contributions of French authors only, even for the period before the war.

HAROLD CUMMINS, Ph.D.

Physical Diagnosis: By Ralph H. Major, M. D. Philadelphia, W. B. Saunders Co., 1945. 3rd ed. rev. Pp. 444. Price $5.00.

By now Major's Physical Diagnosis has established itself solidly as a worthwhile text book in teaching this important subject. A third edition seems to bear out this opinion and a perusal of the book is quick to give the reason for its success. This third edition presents no tremendous changes in the contents of the former two. Additions, alterations, and changes in former points of view, of a minor but nevertheless important nature, characterize this latest book. When a publication has been before the profession for nine years, it is no longer necessary to detail its contents. It is still with all its defects the best modest sized volume that we have at this time.

I. L. ROBBINS, M. D.

The Extremities: By Daniel P. Quiring, Ph.D. Lea and Febiger, Philadelphia, 1945. Pp. 117, 106 engravings. Price, $2.75.

This small book consists of diagrams of the muscles which act on the extremities. No attempt is made to show the relationship of the muscles to each other. However, the nerve supply, blood supply and primary function are given in addition to the principal origin and insertion.

Although this book will serve those who wish to review anatomy or those who wish to refresh their memories concerning a particular muscle, it does not contain enough about each muscle to make the review comprehensive. The fact that the motor point of each muscle is given should make it useful to those who are learning muscle stimulation tests and those who do them infrequently.

The references to the standard texts, Gray and Cunningham, have been carefully kept and should assist the reader to find the details which have been missed in this series of drawings. This book can be recommended to those who wish a hasty review and to those who have need to learn the motor points of muscles.

FRED S. MARSHALL, M. D.

Clinical Parasitology: By C. F. Craig and E. C. Faust. Lea and Febiger, Philadelphia, Pa. 4th ed. 1945. Pp. 871, 305 engravings and 4 colored plates. Price $10.00.

The fourth edition of this well established book has been enlarged somewhat over the previous edition. The section on arthropods and human disease now includes a more comprehensive consideration of the arthropod-borne diseases as well as of their vectors. In most instances the authors have, with characteristic thoroughness, incorporated the important recent contributions and advances in the field of medical parasitology during the war years up to the time of publication. To mention a few examples, it includes information derived from the experience of the armed forces with filariasis, recent data on dengue and sandfly fever, and mentions the uses of the insecticide DDT in insect control and the improved insect repellents. This edition unfortunately does not note the change in dosage of atabrine for the treatment of malaria which resulted from studies of the pharmacology of the drug and recognition of the relation of the plasma level of atabrine to its therapeutic activity. However, it is pointed out in the text that suppressive atabrine therapy with proper dosage has been found adequate to cure practically all *P. falciparum* infections but is not similarly effective for *P. vivax*. The final section which contains important references to the literature in clinical parasitology is exceedingly helpful for the student or individual who desires to seek more information on any particular subject. It is an excellent and authoritative coverage of the subject of clinical parasitology.

J. C. SWARTZWELDER, M. D.

Common Ailments of Man: Edited by Morris Fishbein, M. D. Garden City, N. Y., Garden City Publishing Co., 1945. Pp. 177. Price $1.00.

In this book are discussed many of the ordinary complaints of man. The subjects are written by accredited specialists in their fields. The articles originally appeared in Hygeia. The material is informative and safe in the hands of the laymen. It is a good book to recommend to patients. It stresses the relief and prevention of diseases and yet is so presented as not to encourage the pernicious practice of self medication.

I. L. ROBBINS, M. D.

Sciatiques et Lombalgies par Hernie Posterieure des Disques Intervertebraux: By D. Petit-Dutaillis and S. De Seze, Paris, Masson et Cie, 1945. Pp. 178.

This monograph from Paris is based on a study of the first 50 cases of sciatica due to ruptured intervertebral disk in which operation was performed by the authors. In general, their conclusions are no different from those of English and Americans on this subject.

The monograph is introduced by a pathogenic and anatomic study and followed by a discussion of the etiology, clinical picture, diagnosis and treatment. Personal statistics punctuate their points in the discussion. The authors have not restricted their discussion to sciatica due to ruptured intervertebral disk but have included compression of the cauda equina as well. They have tried to call attention to the fact that herniated disks are responsible for many neuralgias which were formerly thought to be due to lumbo-sacral vertebral anomalies.

The text is generously supplemented with illustrations and a comprehensive although not complete bibliography is appended. The lack of an index does not interfere with intelligent use of the material as the subject matter and its corresponding pagination are clearly indicated in the table of contents.

DEAN H. ECHOLS, M. D.

The Falling Sickness; a History of Epilepsy from the Greeks to the Beginnings of Modern Neurology: By Owsei Temkin. Baltimore, Johns Hopkins Press, 1945. Pp. 380. Price $4.00.

Epilepsy is one of several chronic disorders which has been spoken of in shame and whispers throughout many centuries of its history; however, epilepsy is regarded as a symptom to be controlled rather than a disease entity.

This most thorough narrative review begins with the ancient Greeks who have left us the earliest western writings on epilepsy, and it continues to the point where the historical perspective ends and the present debate begins about the year 1880.

There is no unanimity concerning the range of the concept of epilepsy, and the nature of the dis-

ease is as yet obscure. There are many organic diseases which may lead to the same syndrome as is manifested in "genuine" epilepsy and it is very difficult, if not impossible, to differentiate between some mild epileptic attacks and certain mild cases of hysteria. The broader the viewpoint, from which epilepsy is studied, the more the condition seems to lose its identity and enter the domain of convulsive states encompassing many "epilepsies" of different origin.

The history of epilepsy is such a complicated maze of confused and conflicting trends that oversimplification as well as unwarranted inferences must be avoided and interpretation of material made the main task.

No one will expect a solution of strictly medical problems in an historical book. Its aim is to attempt to elucidate the past and thereby try to understand the selling of present issues.

This book is well organized, thoroughly integrated and tremendously informing and its production is a high-level performance.

C. P. MAY, M. D.

PUBLICATIONS RECEIVED

The Commonwealth Fund, New York: The Modern Attack on Tuberculosis, (Revised edition) by Henry D. Chadwick, M. D. and Alton S. Pope, M. D. Medical Services by Government, by Bernard J. Stern, Ph. D.

Grune & Stratton, New York: Current Therapies of Personality Disorders by Bernard Glueck, M. D. Treatment by Ion Transfer, by D. Abramowitsch, M. D. and B. Neoussikine, M. D. Skin Diseases, Nutrition and Metabolism, by Erich Urbach, M. D., F. A. C. A.

The Johns Hopkins Press, Baltimore: Studies on Brazilian Anophelines from the Northeast and Amazon Regions, by O. R. Causey, L. M. Deane and M. P. Deane.

Lea and Febiger, Philadelphia: The Diagnosis and Treatment of Pulmonary Tuberculosis, by Moses J. Stone, M. D. and Paul Dufault, M. D., F. A. C. P.

J. B. Lippincott Company, Philadelphia: A Bibliography of Infantile Paralysis 1789-1944, edited by Morris Fishbein, M. D., compiled by Ludwig Hektoen, M. D. and Ella M. Salmonsen. Surgical Treatment of the Nervous System, edited by Frederic W. Bancroft, A. B., M. D., F. A. C. S. and Cobb Pilcher, M. D., F. A. C. S.

MacMillan Company, New York: Atlas of Surgical Approaches to Bones and Joints, by Toufick Nicola, M. D., F. A. C. S.

Mead Johnson & Company, Indiana: Monograph on Protein Nutrition (Reprinted from J. A. M. A.). Medical Books Published During 1945.

The C. V. Mosby Company, St. Louis: Pneumoperitoneum Treatment, by Andrew Ladislaus Banyai, M. D., F. A. C. P., F. C. C. P.

Philosophical Library, Inc., New York: Narcotics and Drug Addiction, by Erich Hesse.

W. B. Saunders Company, Philadelphia: Electrocardiography in Practice, (Second edition) by Ashton Graybiel, M. D. and Paul D. White, M. D. Diseases of the Skin, (Third Edition) by George Clinton Andrews, A. B., M. D. A Textbook of Gynecology, (Fifth Edition) by Arthur Hale Curtis, M. D.

Charles C. Thomas, Springfield, Illinois: The Surgical Technic of Abdominal Operations, Fourth Edition, by Julius L. Spivack, M. D., LL. D.